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DR. HARLOW BROOKS, *President*.

TYPHOID ABSCESS OF THE THYROID GLAND. A CASE RESEMBLING CHORIONIC EPITHELIOMA.

RICHARD WEIL, M.D.

DR. R. WEIL presented a case of typhoid abscess of the thyroid gland which he considered of interest not only because of its rarity, but also because it illustrated certain biological peculiarities of the typhoid bacillus. The patient had had a fistula on the right side of the neck for

four years with constant discharge. He had been treated at various hospitals with injections and scraping without success. Dr. Kammerer finally decided to make a complete excision. The fistula ran for a considerable distance to the thyroid gland. At the operation one lobe of the thyroid was removed. In this was situated an abscess cavity about the size of a walnut. The walls were calcific, and contained some thin, purulent fluid. From this fluid a pure culture of typhoid bacillus was recovered. Upon inquiry the patient admitted that the swelling of his thyroid had begun to develop shortly after an attack of typhoid fever four years before. The patient had also when young suffered from goiter, as nearly all such patients have. In the literature Dr. Weil had found ten cases of thyroid abscess after typhoid fever. Of these three were closed and contained typhoid bacilli in pure culture. There was only one case in the literature in which after a long lapse of time an open abscess cavity contained the typhoid bacillus in pure culture. In this case, reported by Parsons in the Johns Hopkins Reports, the bacilli were isolated from a costal abscess after a fistula had been present for three months. Although morphologically and culturally the organisms present in Dr. Weil's case corresponded to the stock cultures they did not respond to the agglutination test. Whereas, the stock cultures reacted to typhoid serum in 1-50, this bacillus reacted only feebly at 1-20. The serum of the patient was examined and was found to have an extremely high agglutinating power, but this also failed to agglutinate the bacteria above 1-20. It seemed possible that this bacillus belonged to the "Ebérthiforme" type of Sacquepée. To prove this the bacillus was injected into rabbits in the effort to produce an immune typhoid serum and so confirm the diagnosis. After cultures had been

transplanted through eight bouillon tubes, the bacillus gained in agglutinating power up to 1-25. It never equalled the stock cultures but still gave what could be called a specific reaction. The immunization experiments were therefore discontinued as unnecessary.

DR. WEIL showed also a case resembling chorionic epithelioma. This was not a true case of chorionic epithelioma but it had given rise to so much confusion in diagnosis that he thought it well to present it. He said that there was of course no difficulty in recognizing certain cases of chorionic epithelioma; that is, cases in which shortly after abortion or delivery a tumor was found in the uterus. There were, however, a series of cases about which a good deal of discussion had arisen as to diagnosis;—those in which after a variable period after abortion or delivery, ranging from months to years, these so-called chorionic epithelioma have been found not in the uterus but in distant organs: those in which these tumors had been found in virgins, as in the case of Lubarsch: and, finally, those occurring in men, angioplastic sarcoma or teratoma of the testicle, which have been described as chorionic epitheliomata. There are also cases such as that reported by Marx, in which tumors were found in the liver, which were similar to these hemorrhagic tumors, but occurred in a man who presented no tumors of the testicle. Marx placed such tumors with the endotheliomata. The case presented by Dr. Weil occurred in a woman of twenty-nine years of age. She entered the hospital practically moribund. Her husband declared that she had not recently been pregnant. At autopsy the uterus and adnexa were found to be perfectly normal. In the stomach there was found a tumor about the size of a navel orange situated near the pylorus, but not causing obstruction, yellowish red in color, and

slightly ulcerated. In addition to this there were tumors in the liver. The liver was found to be studded with large hemorrhagic masses which were reddish brown in color and varied in size from a pea to an orange. They were fairly sharply circumscribed and looked exactly like the metastases of chorionic epithelioma. The other organs were entirely free from invasions. Microscopical examination showed that this was a case of primary tumor of the stomach, with metastases in the liver. The muscularis and submucosa contained small nodules composed of adenomatous strands of cylindrical cells. These lay in a cellular stroma composed of epithelioid cells. The stomach tumor might without doubt be classed as an adenocarcinoma, somewhat atypical in the fact that the adenomatous structure had been to a certain extent replaced by a diffuse proliferation of epithelioid cells. These nodules even in the stomach showed hemorrhagic areas. There was also invasion of the blood vessels in the wall of the stomach by tumor masses. The tumors in the liver were intensely hemorrhagic, and it was difficult to unravel their histology. At the periphery of the masses of clotted blood which formed the center of these metastases, one could see collections of large, lightly staining, epithelioid cells resembling closely those observed in the primary tumor. No adenomatous structures could be discovered. Microscopically, therefore, the tumor bore certain resemblances to chorioepithelioma. The presence of syncytium in the tumor was to be excluded, although closely simulated by degenerating cords of liver cells which were to be found amid the tumor masses and in which the cell boundaries were quite wiped out. The only case in the literature to which comparison could be made was that of Marx, in which syncytium (of doubtful authenticity) was also found in the tumors in

the liver. His case would also have been diagnosed as chorionic epithelioma had it not occurred in a man in whom there was no teratoma of the testicle. It is, therefore, quite evident that this type of tumor may be closely simulated by other tumors of very different origin, if they are hemorrhagic and contain large epithelial cells. The presence of pseudo-syncytium especially in the liver, is frequently an additional source of error. But even true syncytium is not characteristic, as was thought by Marchand, of foetal tissues, but may occur in any carcinoma or endothelioma. On this basis, Sternberg presented a teratoma of the testicle containing syncytium at the last meeting (1904) of the German Pathological Society, but refused to regard it as chorioepitheliomatous tissue. The actual character of all those tumors hitherto grouped in this class but not occurring in undoubted consequence of a pregnancy must, therefore, be carefully reconsidered; the diagnosis is no longer so simple as was once believed.

Discussion.

DR. W. H. PARK said that he had been interested in the report of the agglutination characteristics of typhoid bacilli which had been living in the body for so long as four years. The low agglutinability on isolation with later recovery after transplantation reminded one of bacilli grown in fresh unheated serum. At the Laboratory of the Health Department Dr. Collins had diminished the height of the agglutinating reaction of bacilli, ninety-five per cent. by growing them for twelve periods of twenty-four hours each in serum. When grown again on nutrient agar they recovered their agglutination characteristics much more slowly than did Dr. Weil's cultures.

DR. C. W. FIELD said, in regard to syncytium in

tumors, that he had showed some time before a primary endothelioma of the peritoneum in a man. In that tumor there was a large amount of syncytium and only the peritonium was involved. No other organs were involved.

DR. HARLOW BROOKS said that he had recently examined material from a woman who declared that she was a virgin, in which the growth was undoubtedly chorionic epithelioma. Some had been inclined to look upon it as one of the growths occurring without impregnation. On examination he had been assured that it was from the remains of placental tissue that the growth originated. Personally, however, he did not believe that one was justified in saying that all these tumors came from either maternal or foetal tissue.

DR. WEIL said that he did not quite understand why an ordinary carcinoma should in this case give rise to intensely hemorrhagic metastatic tumors. It was easy to understand the formation of such tumors in the endo- and peritheliomata, which were essentially vascular tumors. By way of explanation, he suggested that in this case the metastases travelled by way of the portal system, and not by the lymphatics, from the stomach to the liver. Sections of the stomach revealed tumor invasion of the blood vessels.

AN EPIDEMIC DISEASE OF TROUT.

CYRUS W. FIELD, M.D.

DR. C. W. FIELD described an epidemic disease of trout occurring in the preserves of the Southside Sportsmen's Club on Long Island. This broke out in the

latter part of October and was first noticed in the early part of November as being very extensive. Dr. Field showed a plan of the preserves. The water passed down from the brook and entering the first preserve bubbled up and became well aerated. On going into the lower preserves it passed through screens and so was not aerated. The disease first broke out in the tanks to one side. No fish in the first preserve and very few of the young fish were affected. Very few fish in the lower brook died of the disease and these had probably been thrown there by the keeper. From the middle of October to the 10th of November, 5,400 fishes died. From that time to the first of December, 2,100 fishes died. In the early part of November the fish were all turned out into the lower brook. The death rate then dropped to 1,600 for December, and 1,000 for January. For the first week in February it was about normal.

The gills of the diseased fish were found to be pure white instead of being a healthy red. In the normal gill large quantities of nucleated red blood cells could be found, but there were none in the diseased gill. On autopsy the only pathological condition present was the liver which was markedly enlarged, very friable, and yellow instead of being brownish red in color. Microscopical examination of the livers of the fishes showed intense fatty degeneration and large areas of necrosis. In the fish the liver is the great hemapoietic organ of the body; the spleen takes very little part, if any. All the other organs were absolutely normal. The ventral artery which in the healthy fish was very large and red, in the diseased fish was simply a gray slaty line, and when smears were made was found to contain slaty detritus. Dr. Hodenpyl had gone to the Club and had had four healthy and four diseased fish placed in a small

tank together. These fish were fed for two weeks on fish dead of the disease. One of the diseased fish died. The four healthy fish when taken out were found to be normal. The remaining three diseased fish showed a pink tint to the gills. Two weeks later the diseased fish could not be distinguished from the healthy ones. Dr. Field had had thirty diseased fish put in one preserve and thirty normal fish in the next preserve. Of the diseased thirty, four or five died. After two weeks only three showed white gills, while none of the normal fish had become diseased. An interesting point was that the disease in these preserves spread against the current, not with it. The fish in the lower brook were not affected, and the diseased fish which were turned out into the brook got well. On Dr. Field's first visit about 50 fish were netted from the brook, and among these were only two healthy fish. Two month's later 50 more were netted and there was not one diseased fish among them, though a few had pale gills. This epidemic occurred at a time when the preserves held three times as many fish as ever before, and when the water supply had been cut down one-half. At the same time a number of fish which had died of ulcers came down from the upper brook. This, however, had nothing to do with the anæmia in the preserves. Cultures were taken from the fish and studied at various temperatures. No bacteria were found except from the ulcerated fish which showed large quantities of a very slender bacillus. A number of rainbow trout, which are a very hardy trout, were in the preserve, and none of these were affected. The disease seemed, therefore, not to be of an infectious nature, but one which was probably due to lack of oxygen in the water. Dr. Field thought this interesting in connection with human anæmias.

Discussion.

MR. SLADE, the President of the Club, said that when the disease first came to his notice he naturally assumed that it was due to the food, but on investigation he found that the fishes had been regularly fed on pig's liver, as they had been for two years. He had thought it possible that some disease of pigs might have caused the epidemic, but the doctors were agreed that the food had nothing to do with it.

DR. HARLOW BROOKS said that he had looked over the sections with a great deal of interest, and he considered that Dr. Field was right in saying that the only lesions present were such as might occur from extreme anæmia. This anæmia was interesting as not having been due to filthy conditions, but simply to a lack of oxygen, although the amount of food had been plentiful. He had while fishing seen fish in shallow, land-locked pools, whose gills were white. Later on these fish were very apt to become infected and covered with whitish parasitic scales. They, however, first showed the signs of anæmia.

A NEW AND PRACTICAL METHOD FOR THE DETERMINATION OF THE COAGULATION OF THE BLOOD.

L. B. GOLDHORN.

MR. L. B. GOLDHORN demonstrated a new instrument devised by Dr. Biffi, of Lima, Peru, for the determination of the coagulation time of blood. The instrument was exceedingly simple and seemed to be very efficient. It consisted of a glass cylinder and a perforated

cork containing a thermometer with the reading above the vessel, and, secondly, of a glass rod or tube in which was fused a platinum wire, bent in such fashion as to have a number of loops which were even in diameter. To use the instrument the jar was filled to the black mark with water. The finger was punctured, note being taken of the time. The loops were touched to the surface of the extruding drop, care being taken that simply the periphery of the drop was touched. The reading of the thermometer was taken. The tube was replaced, and after five minutes the rod was pushed down and the first loop introduced into the water. If no fibrin formation had taken place the blood dissolved completely and the loop became perfectly clear. After another lapse the second loop was pushed into the water, etc. When fibrin formation started it could be seen immediately that there remained a slightly tinged remnant of coloring matter in the loop. When coagulation was complete the loop showed a solid red mass. The instrument was so simple that any one could make it. The coagulation time depended in the first place upon the temperature of the air and of the water, and on the size of the loop. It would be desirable to have a thermometer which would take a reading of the water so as to obviate temperature changes in the vessel. Dr. Biffi had suggested that the loop be a single twist in the wire. Mr. Goldhorn had found, however, that this was not permanent and not very desirable because by capillarity the blood went to the point where the two wires crossed and this caused a slight difference in the coagulation time. Mr. Goldhorn made his loops more permanent by giving an extra twist so as to have the loop unalterably fixed on a little stalk. To clean the instrument it was only necessary to take out the platinum wire hold it in a flame, and, if necessary, cleanse it with acid.

The size of the loop had considerable to do with the coagulation time. The smaller the loop the more rapid the reading obtained, but there was also a greater error because it was much more difficult to get a uniform amount of blood in a series of small loops than in a series of large ones. The instrument should be a very useful one, and should be put on the market. Mr. Goldhorn said that the instrument had already shown him many things. He had recently seen a case which had been pronounced undoubted hæmophilia. The coagulation time would be supposed to be very much diminished, but as a matter of fact, by this instrument the time was very much increased. It had also shown him that there was no relationship between the coagulability or fibrin formation and the blood plates.

Discussion.

DR. J. H. BORDEN asked Mr. Goldhorn whether he had tried to find the limits of coagulation time by this instrument and whether he had made any tests to determine how it corresponded with other methods.

MR. GOLDHORN said that Dr. Biffi had found that the instrument as made by him corresponded in time with other methods. It all depended upon the temperature and the size of the loop. Dr. Biffi had suggested that the loops be 3 to 4 mm. in diameter and 1 cm. apart, and he then found that at a temperature from 20 to 25° C., coagulation was complete in from 7 to 10 minutes in a normal subject. With the instrument as shown it took about twice as much time, but this was necessarily more accurate on account of the larger size of the loops.

DR. W. H. PARK gave a short report of work done under his general direction by Mrs. G. Van Everen Stoughton, with the colon bacillus. The work was undertaken to see to what degree members of the colon group taken from a great number of cases, normal and diseased, were alike in their agglutination characteristics and their fermentation of sugars. Mrs. Stoughton tested fourteen cultures from different persons by injecting them into rabbits. Some animals received three organisms, some seven, and others only one. It was found that organisms derived from different cases but apparently the same, reacted very differently with the same serum. With the sera obtained tests were made of various cultures. Only a few cultures of those which had not been injected into the special animal whose serum was being tested agglutinated even slightly. This did not harmonise with the belief that most cultures of *B. coli* react to some of the different specific agglutinins for the colon bacillus. For instance, rabbit I was injected with cultures of cases 1, 7 and 12. The other eleven of the fourteen cultures did not react even 1-20 with this serum. Rabbit II was injected with 3, 4 and 10. Culture 3 reacted 1-200; 4 and 10, 1-500. Strains 1 and 2 gave a fair reaction at 1-20. The other nine gave no reaction in 1-20. Rabbit III was injected with 2, 8 and 13. Culture 2 reacted 1-300; 8, 1-500; and 13, 1-200. Strains 1 and 7 gave a fair reaction in 1-20. The other strains gave no reaction or only a slight one. Thus, with fourteen organisms, probably rather more distinct than usual, not one gave rise to any appreciable specific agglutinins for the others. Large numbers of colon bacilli—44 from different cases and 50 consecutive colonies from one plate—were taken and tested on different sugars. With the ordinary tests with dextrose, indol, etc., these all re-

acted alike except for the amount of gas produced. When saccharose was tried it was found that $\frac{1}{3}$ did not ferment saccharose with the formation of gas. Of those that did, a portion caused no increase of acid in the sugar broth. In the bacilli from different cases there was a very marked difference in the amount of gas, from 15 to 90 per cent. being produced in the fermentation tubes. The whole work went to show the enormous number of varieties of bacilli which are included in the colon group.

Discussion.

DR. E. LIBMAN said that he had been interested for some time in the question of agglutination of the members of the colon group. He had found a great deal of difficulty in establishing definite relationships in the colon group. Often groups which culturally were identical would not agglutinate at all similarly. He thought that in future experiments with members of the colon group derived from the intestinal tract, it would be wise to test the agglutination after they had been withdrawn from an animal upon which they had exerted some pathological effect. While the bacillus might then be agglutinated to a certain extent, that reaction might be entirely lost in a few days. He had seen an example of this when working with a paratyphoid bacillus. The organism had first been isolated from the gall bladder and the serum gave a thread reaction with this bacillus. It was next isolated from the blood, and the serum then gave a thread reaction with the organism from the blood, but only an agglutination with the organism from the gall-bladder. Two days before death it was again isolated from the blood, and the serum then gave a thread reaction with this last, an agglutination with the first organism isolated

from the blood, and no reaction at all with the organism from the gall-bladder. He thought, therefore, that it would be advisable to test the organisms directly after they had been passed through an animal.

DR. PARK said that Dr. Libman's remarks and the results which all get in their work with these organisms showed how much these bacteria vary from time to time. Most of the agglutination tests in laboratories had been done with stock cultures growing on artificial media. He thought it was easy to realize that a bacillus passing from the gall-bladder to the blood might change rapidly in its specific properties as it developed. Bacilli taken on successive days might present entirely different characteristics. The bacilli as they increased in the body fluids would vary greatly in their offsprings, since those least susceptible to the bactericidal substances of the blood would be the ones which developed.

SOME OBSERVATIONS ON THE EFFECT OF SYMBIOSIS ON THE GROWTH OF THE STREPTOCOCCUS MUCOSUS CAPSUL- ATUS AND CERTAIN PNEUMOCOCCI.

LEO BUERGER, M.D.

I wish to show a few plates which demonstrate the growth of the *Streptococcus mucosus capsulatus* and certain pneumococci, in symbiosis. The observations which I wish to bring to your notice were made while studying the bacterial flora in the mouth of a normal individual. About seventeen days ago some plates which I had made from the mouth secretion of a normal case

were found to be studded by numerous colonies of the streptococcus mucosus. These colonies varied in size from two to three mm. in diameter. Sub-cultures were made, the organism identified, and the plates were allowed to stand at room temperature. Three days later the plates were again taken up for study. It was then noted that other colonies had appeared. These were very large, five and even six mm. in diameter, of a mucoid appearance, resembling to some extent the colonies of very luxuriously growing Friedländer bacilli. Some of them were discrete, while others had increased so rapidly in size that they formed large confluent masses of slimy surface growth. The discrepancy in size between these colonies and those ordinarily found in the case of the Streptococcus mucosus, made me at first think that I was dealing with a different organism. Sub-cultures, however, showed conclusively that the organisms were identical. In attempting to explain this marked increase in the size of the colonies, I again examined the old plates and now observed that whereas the old colonies of the Streptococcus mucosus as a rule present no dense center, all the large colonies presented a more opaque, whitish center. Although spreads made from the superficial portions of the colonies, twenty-four hours previously, had shown only streptococci, I was now led to think that perhaps the presence of some other organism had favored the development of the streptococcus. I accordingly picked off portions of these denser and more opaque centers and found that they were composed of Gram negative bacilli.

In order to prove that the presence of these bacilli was instrumental in causing the luxuriant growth described, I have made a few experiments which have shown conclusively the correctness of this view.

Work in other directions did not leave me the time

to make an extensive study either of the bacillus or of its effect upon the growth of many organisms under varied conditions. I will give you merely a short résumé of what has been found so far.

The bacillus itself is rather large, broad, non-motile, Gram negative, and tends to assume the diplo-bacilloid form. In recent cultures the double forms prevail, and the elements are comparatively short. In other growths, more of the longer single forms are to be seen, and the tendency to involution is very great. It grows poorly on acid media unless they contain glucose (other sugars have not been tried) or serum or broth. The neutral titer seems to be most favorable for its development. The best growths were obtained on glucose serum agar or glucose serum broth. Fairly large doses have not proven pathogenic for either mice or guinea-pigs. Up to the present time I have not been able to identify this organism.

The demonstration plates, which I wish to show you, will illustrate the effect of symbiosis on two strains of the streptococcus mucosus and two strains of the pneumococcus. The original plates show the smaller colonies of the streptococcus and the large mucoid, translucent masses with the opaquer and denser central areas. The centers have increased somewhat in size, so that they now form an appreciable part of the base of the mass. However, by far the greater part of these colonies is composed of mucoid material made up only of streptococci.

Plates of glucose serum agar were streaked with the streptococcus mucosus isolated from the above mentioned case, and another similar organism derived from another source. After twenty-four hours incubation, small quantities of cultures of the bacillus were admixed, care being taken to avoid spreading of the colonies over

sterile portions of the plate. In twenty-four hours the streptococcus growth almost doubled its size on the plate, whereas the growth of the bacillus occupied but a very small portion of the total mass. The increase in size of the former takes place fairly rapidly even at room temperature, whereas under ordinary conditions its growth without incubation is poor. It is interesting to note the overgrowth of the streptococcus. The consistency of the colonies also becomes altered. They become more mucoid and stringy, so that it is difficult to remove portions for examination.

Other plates showing discrete colonies to some of which the bacillus had been added showed the same result.

If the procedure be reversed and the streptococcus planted on a colony of the bacillus, the effect is not so marked. There is some increase in size of the streptococcus growth but it falls far from attaining the luxuriance of the streptococcus under the other conditions.

Two strains of the pneumococcus were also experimented with. The particular organisms selected were both rather unique in their luxuriance and rapidity of growth. When grown in symbiosis with the bacillus, they also produce large mucoid colonies of considerable dimensions. The viscosity of the surface growth was found greatly increased as in the case of the streptococcus.

It is interesting to note in this connection that the case from which these organisms were isolated was kept under observation for a period of two weeks, during which time three strains of the bacillus and four of the *Streptococcus mucosus* were isolated on four different days. Perhaps the persistence of the streptococcus in

the throat of this normal individual was influenced to some extent by the presence of the bacillus.

I have not as yet studied the effect on the growth of other pneumococci and streptococci. Experiments in this direction may possibly be of value in demonstrating differences not brought out in other tests.

Discussion.

DR. W. H. PARK asked Dr. Buerger whether he had tried injecting this bacillus with pneumococcus or streptococcus into animals to increase the virulence of these organisms.

DR. BUERGER said that he had not.

A COMPLEX CASE OF MULTIPLE CYSTS OF THE LIVER.

HARLOW BROOKS, M.D.

DR. BROOKS demonstrated a complex case of cysts of the liver, showing it in connection with the previous cases shown by Drs. Moschcowitz and Weil. This case admitted of almost any explanation of the nature of the cysts. The history of the case was unimportant except that the man was a degenerate, mentally, morally and physically. He was also probably syphilitic. The chief anatomical findings were: Hyperplastic pneumonia with gangrenous ulcerated and papillomatous enteritis, with double inguinal hernia and beginning intestinal cancer; interstitial nephritis with cysts of the kidney; necrosis of the testicles and acute cystitis; chronic meningitis with a very primitive development of the brain cortex; and multi-

ple cysts of the liver. The brain was very interesting; in its cortical development it had not risen even as high as the type of the chimpanzee or orang. Mentally the man was about at this level. There was no clinical history nor sign of hepatic disease. When the liver was removed the duct of the gall-bladder was found freely open. It contained about the ordinary amount of bile. The entire substance of the liver was mottled with small greenish-walled cysts, but they contained perfectly clear mucoid fluid, not bile stained. The cysts varied in size from 1 mm. to 1 or 2 cm. They were as a rule in the interlobular spaces, but some were in the centers of the lobules. This might be explained by the fact that some showed well marked diverticula. Dr. Brooks thought this might be considered as a congenital cystic condition. This was borne out by the fact that the man was a congenital degenerate in many ways. Dr. Prudden had called attention to the fact that if one congenital lesion were present others would also usually be found. On the other hand, it might be looked upon as an adeno-carcinomatous growth. The case presented a great many points which admitted of discussion.

Discussion.

DR. R. WEIL said that the question of adenoma, which always came up in such cases, was very puzzling. It seemed to him that there were a great many things against such a theory. It was rather curious that this condition almost invariably occurred in association with other congenital lesions. The fact that practically the entire liver was uniformly permeated by the change was another argument against adenoma. There was, further, no active proliferation of the so-

called tumor tissue. Dr. Weil considered it to be an anomalous congenital condition of the epithelium throughout the entire organ. In the bile ducts there was a condition resembling adenoma, but when one considered the entire organ and the fact that this occurred with other congenital lesions, Dr. Weil did not see what ground there was for the theory of adenoma. There was the additional factor of adenomatous tumors at the bases of the ulcers, but one would hardly be inclined to regard these small isolated cysts as metastases. Their formation owing to occlusion of the bile ducts hardly entered into this particular case because there was no cirrhosis.

DR. E. MOSCHCOWITZ thought that the assumption of a congenital origin did not entirely explain the microscopical lesion. He thought that in addition another factor played an important part in the pathogenesis.

DR. BROOKS said that he wished to confirm Dr. Weil's statement that there was no cirrhosis present, so that one could strike out inflammatory growths of the bile ducts.

THE IDENTIFICATION OF THE PNEUMOCOCCUS IN BLOOD CULTURES.

THOMAS FLOURNOY, M.D.

DR. THOMAS FLOURNOY described a characteristic appearance of the pneumococcus which he had seen in his work. Although made independently, his observations could only be taken as corroborative of Schotmüller's and of Rosenow's, which had appeared previously. In the course of a number of blood cultures

made upon cases of lobar pneumonia it was noticed that colonies of the pneumococcus developed a brilliant green color in blood-agar plates. The blood cultures had been obtained by inoculating one c.c. of blood into a tube of melted agar and plating at the bedside of the patient. In this way a uniform mixture of blood and agar was obtained. The specimens were chiefly from severe, well-marked cases of lobar pneumonia. One was from the blood of a case of meningitis which was due to the pneumococcus. From the plates inoculations were made into other media and into mice. The green color was constant in the colonies of all these cases. It was seen best macroscopically and by transmitted light, but could also be seen under the microscope. The bacteria isolated in the cases mentioned were all fairly easy of identification by the ordinary cultural and staining methods. No work had been done on more doubtful strains. Apparently, however, the pneumococcus in a mixture of blood and agar develops a color not found with the ordinary pathogenic cocci. The explanation of the development of this color might possibly lie in some process comparable to the breaking down of old hemorrhagic foci in the body.

Discussion.

DR. E. LIBMAN said that he had noticed the phenomenon but had not made many tests himself as most of his pneumococcus work was done on fluid media. It seemed that it was a method which was worthy of further trial because it would be a very rapid means of diagnosis, particularly if combined with some of the newer capsule stains.

A PRELIMINARY REPORT CONCERNING THE EFFECT OF THE X-RAYS ON KARYOKINESIS.

HARLOW BROOKS, M.D., AND L. B. GOLDHORN.

DR. HARLOW BROOKS said that he had only a few words to say on the work which he and Mr. Goldhorn had been doing, because they had so far found only a few things of definite character. The investigation had been suggested by a presentation of Dr. Tilden Brown's a few weeks ago, before the Section on Genito-Urinary Diseases, in which he stated that in one hundred per cent. of the cases in which he had investigated the spermatic secretion of X-ray operators he had found absolutely no spermatozoa. The results of the few cases examined by the speaker confirmed this. Investigations were carried on to find what changes led to this absence of spermatozoa. Rats were selected for the experiments on account of the fact that in these animals spermatogenesis takes place very actively. So far the animals had been exposed only to the deep penetrating ray; that is, the ray which is designed to effect the deeper structures. Exposures were made for from fifteen to twenty minutes daily up to eighteen days. So far the results had been only very suggestive. Plates were shown indicating some of the changes found. At first exposure to the X-ray greatly excited the secretion of spermatozoa, and, if anything, they were rather more active than normal. Although much work was still to be done, they felt confident in saying that the X-ray increases the production of spermatozoa; that the X-ray after a considerable number of exposures does cause certain degenerative changes in the cytoplasm of the cells; that the X-ray does excite marked changes in the chromatin of the spermatocytes.

So far the changes were not distinct enough to allow of conclusions being drawn from them. They were like changes found in a lesser degree in the normal. Later on karyokinetic changes took place which, it was believed, eventually resulted in the destruction of the chromatin of the spermatocytes and the formation of spermatozoa deficient in chromatin or entirely lacking heads.

Discussion.

DR. JAMES EWING inquired whether Dr. Brooks had any intention of using radio activity as well as simple X-ray treatment. As he understood the nature of radio activity and X-rays, there were at least three forms of energy manifested. One of these was concerned with the emanation of a gas which was more active on the tissues. Did Dr. Brooks intend to employ all three forms of radio activity?

DR. BROOKS said that so far they had found their studies so much more difficult than they had anticipated that they had no desire to undertake anything more. They had found great difficulty in carefully controlling the experiments. Many things had been seen in supposedly normal testicles which had not been before described.

THE PRACTICAL VALUE OF R. STERN'S BACTERICIDAL TEST OF TYPHOID SERA.

MARY E. GOODWIN, M.D.

DR. GOODWIN gave a short account of her experiments with the above test, prefaced with an abstract of Stern's work.

R. Stern, of Breslau, after examining the blood of fifty-nine typhoid, and ninety non-typhoid cases for its bactericidal power on typhoid bacilli, decided that the bacilli were destroyed by much higher dilutions of the typhoid blood than of the normal.

He found no fixed relation between the day in the disease when the blood was taken and the amount of immune body it contained. He gives as his strongest serum one which showed a decided reaction in a 1-4,000,000 dilution. The earliest day on which the bactericidal power was marked was the eighth, in one case the serum reacting in a 1-40,000 dilution and in another in a 1-4,000 dilution. The agglutinating power of the typhoid sera was not shown in nearly as high dilutions as the bactericidal power. He concludes by saying that the higher the dilution showing bactericidal action the greater probability of the case being typhoid.

His technique is in brief as follows:—After inactivating the sera at 55° C. for 30 minutes, he makes the dilutions with 0.85 per cent. salt solution. For the complement he takes fresh rabbit serum in a dilution of one part to eleven of salt solution. The typhoid culture used was one which had been isolated about one year and was of moderate resistance, he having found that those recently isolated were too resistant, while the old cultures were killed by the rabbit serum alone. He put together in small test tubes 1 c.c. of the serum dilution, $\frac{1}{2}$ c.c. of a 1-5,000 dilution of a twenty-four hour bouillon typhoid culture in bouillon and $\frac{1}{2}$ c.c. of the diluted rabbit serum, always using as a control, 1 c.c. of salt solution with $\frac{1}{2}$ c.c. of diluted culture and $\frac{1}{2}$ c.c. diluted rabbit serum. His control he plated from immediately, then put all the tubes at incubator temperature for two to four hours. At the end of that time he plated them all in agar, incubated the

plates and counted after 12 to 18 hours. All of this process Stern says can be done in one half hour for one serum and the time reduced when more than one serum were tested at the same time.

In testing 27 typhoid sera and 7 normal sera in the Board of Health Laboratory Dr. Goodwin had found the test more difficult than the general tone of Stern's article suggested. The rabbit serum differed so much in its immune body content that sometimes it was necessary to test several rabbits before finding one that would not destroy too large a proportion of the bacilli added. After several failures a Mount Sinai Hospital culture and a New York Hospital culture which seemed to be suitably resistant were found. Among the few cases examined no serum was found of such unusual strength as Stern's which showed the decided reaction in a 1-4,000,000 dilution. None of the sera showed a reaction above 1-200,000; the highest dilution of a normal serum showing a reaction was 1-100. The earliest serum tested was from a ten day typhoid. A 1-500 dilution gave a plate of 8,000 colonies while the normal serum control contained 100,000 in the same dilution. The bactericidal power was found in much higher dilutions than that of the agglutinating. It took much longer time to make the test, about two hours for a single serum and an hour for each additional one. The test seemed too complicated for routine laboratory work but of undoubted value in obscure cases where a diagnosis could not be made. The full value of the results can not be estimated until work has been done on obscure cases of colon and dysentery infection where one might be misled by the large amount of common immune body present.

Discussion.

DR. W. H. PARK said that during the course of the work experience had been gained which seemed to him of some interest. The first results had been very disappointing. After reading Stern's first article the technique seemed to be very simple. Specimens of serum were taken from six typhoid cases and from four normal persons, so as to get a rough estimate of the value of the test. The making of the tests took a full day. On the next morning it was found that the culture used was so sensitive that the rabbit blood alone had killed all the bacilli so that the plates were sterile. For a moment it seemed as though the test were a failure, but Dr. Steinhart suggested that some other culture might show just sufficient resistance to resist the rabbit blood, but be killed by the addition of a typhoid patient's serum. The Mount Sinai culture obtained from Dr. Libman was then tried and found to be of about the right resistance. A second point of interest was that during the course of four or five months this culture has shown no change and probably would never become as sensitive as the one first tried. Dr. Park thought that even in his second paper Stern made the test appear much simpler than it really was. However, with suitable culture and great patience Dr. Goodwin had obtained results which, though not as definite as Stern's, indicated that the test might be of value in doubtful cases. Only a large number of tests could establish this. Dr. Goodwin would be very glad if any one who had a doubtful case would send her some serum for testing.

CONCERNING THE CAUSES OF GALL-STONES.

EDWIN BEER, M.D.

My purpose in presenting this short paper to this Society is twofold: First, I wish to indicate a new method of investigating a very difficult problem, the causation of gall-stones, and to show what results this new method of investigation has borne in my hands; secondly, I wish to interest the members of this Society who are in a position to examine organs derived from a large number of autopsies in this method of investigating, so that more cases may be brought together and studied, and the correctness of my data be either verified or denied.

Without going into the earlier history of the theories of gall-stone production which would lead us far astray and tend to obscure the points that I wish to emphasize, I would like to unfold to you the development of the present theory of gall-stone production. This development is closely bound to the Strassburg school of medicine, to Naunyn and his pupils. The work of this school gave us our present conception of the etiology of gall-stones.

Before the publication of these modern views the whole question of gall-stone production was unsettled, just as unsettled as the question of etiology of pulmonary consumption prior to the discovery of Koch's bacillus. Diathesis, heredity, age, sex, were regularly named as the causes of cholelithiasis, while the actual processes at work were scarcely considered. In the early 90's Naunyn attacked these time-worn causes, and he applied all his energies to the annihilation of the diathetic theory and to the building up of a new theory based on bacteriological facts. As was perfectly proper and logical he set to work

to determine the origin of the substance found in gall-stones. Bile pigments, cholesterin, and the organic frame-work had to be studied and investigated. He had to determine whence they came, under what conditions they were produced, whether they were increased or diminished by changing the conditions of the experiments. In this work Kausch, Thomas, and Jankau were of great assistance. From the data furnished by these experimenters, Naunyn concluded that the solids in bile are independent of general body conditions; that cholesterin is a product of the bile passages, and as such is not influenced by any diathetic or non-local conditions; that bacteria enter the bile system, set up an inflammation, catarrhal in type, which blocks the free outflow of bile, and which is accompanied by an increased production of cholesterin from the inflamed mucous membrane of the gall-bladder, and *parri passu*, an exudation of albuminous substances. In this bacterial catarrh all the elements of the gall-stones are present, and by processes of precipitation and infiltration stones develop absolutely independently of the general body conditions.

When this view was published no convincing experiments were put forth to establish the positive fact that infection of the bile passages actually produced gall-stones. That work was reserved for others, and a number of years elapsed before this evidence was furnished. Mignot and Miyake succeeded in producing gall-stones experimentally in animals by partially occluding the cystic duct, thus producing incomplete stagnation of the bile, and then introducing bacteria into the gall-bladder and causing an inflammation of this organ. This work gave the firm support that Naunyn's theory had lacked when it was originally published. Since Mignot and Miyake did their work, others have repeated the experiments with varying

results, but nobody seems to have tried to follow and analyse the genesis of stones in the human body.

It seemed to me that if certain cases could be studied, we would be in a position to trace the development of gall-stones in the human body. To obtain the same or similar conditions to those of the experiments of Mignot and Miyake I would have to get livers in which there was stagnation of bile and infection of the bile passages, as the gall-bladder in acute inflammatory conditions rarely comes to the post-mortem room unopened. Patients are either operated and the bladder is emptied or they get over the acute attack, and we know not what has occurred in the bladder. The few that die of this condition represent the most acute cases, and as they are of short duration only, the study of stone formation is practically impossible because of the early stage of development of the stone. These facts turned my attention to the liver and its ducts. Here we find obstructions and inflammatory conditions combined. Here in cases of common duct obstruction and secondary cholangitis the conditions obtained by the animal experimenters were paralleled. In these cases, which unfortunately for this investigation, are very rare, nature reproduces the conditions that Naunyn thought underlay the process of gall-stone production. The conditions are purely local. There is stagnation of bile and there is inflammation of the mucous membrane of the bile passages. If it were possible to obtain a sufficiently large number of human livers with the above conditions present, the correctness of Naunyn's views as well as the direct applicability of the results of animal experimentation might be verified, and the theory of gall-stone production in human beings would rest on a firm basis.

I was able to collect eleven cases at autopsy¹ in

¹ Similar clinical and operative cases taken from the literature are to be found in a paper on "Intrahepatic Cholelithiasis" written by me. *Medical News*, 1904.

which there had been a common duct obstruction for more than four or five weeks, and in which a more or less severe inflammation of the extra and intrahepatic ducts had developed. In seven of my cases the common duct was obstructed by calculi, in four by tumors of various kinds. In the first series of seven cases, as a result of the conditions of the experiments, stones formed in the liver ducts. In the second series of four cases, though apparently the same conditions were present, no stones developed, though stagnation of bile and inflammation of the mucous membrane of the bile passages were present. In this second series Naunyn's causes were present just as in the first series, but no stones developed. How are we to explain this difference? Why should gall-stones be produced in the liver ducts in one series and not in the other? Is it mere chance that cases with previous cholelithiasis regularly showed stone formation in the liver ducts when common duct obstruction due to stone and cholangitis developed, while those that had no previous stone formation did not develop stones when stagnation of bile and cholangitis developed?

The absolute regularity in the results seems to me to preclude chance, and even though my series of cases be small I think it points to a new factor in the production of gall-stones. It is needless to theorize at this stage as to what this factor may be. If to make my point clearer we call the third factor an altered liver metabolism or a diathesis, we could understand why stones developed in the liver ducts when stagnation and infection developed in cholelithiasis cases, they having the predisposition as evidenced by the older stones, and why they would not develop under similar conditions (second series) where no liver disturbance and no diathesis were present. But the term diathesis is vague and

almost meaningless, and merely a garb for ignorance. Perhaps a faulty hepatic metabolism underlies the formation of gall-stones? A larger material bearing on this subject could readily be gathered by the members of this Society without entailing any great trouble and a larger material would help to clear up this difference that I have described between the cases of old cholelithiasis and those without cholelithiasis. And as I said at the outset it was with the purpose of enlisting your assistance that I read this paper.

In closing, I may sum up the results that I have obtained as follows:—

a, Naunyn's factors—stagnation of bile plus inflammation of the bile passage mucosa—do not seem to be sufficient by themselves to lead to gall-stone formation even though the time allowed for the working of the causes be adequate.

b, My first series of cases shows that these two factors lead to stone formation in patients who previously had gall-stones. In these series we have the first real evidence of the factors underlying gall-stone production and the causes of cholelithiasis.

Discussion.

DR. OTTO H. SCHULTZE said that among the cases which came to the Morgue, in which gall-stones were rather common, the same thing had been shown as mentioned by Dr. Beer; namely, that in some cases of compression of the common bile duct where inflammation had taken place and every opportunity had been given to the factors mentioned by Naunyn, no gall-stones were found, and in some cases where gall-stones were found the common bile duct and the ducts throughout the liver seemed

to be quite normal. When stones were present in the bladder it seemed to him as likely that the stones caused the inflammation as that the inflammation was a factor in producing the stones.

DR. CHARLES NORRIS said that so far as his experience went he quite agreed with Dr. Schultze. The gall-bladder was frequently found to contain stones when there were no signs of previous inflammation. In old cases there was often a thickening of the wall of the gall-bladder.

DR. E. LIBMAN said that he could not speak positively concerning his cases without consulting the records, but his general impression was that the material ran as Dr. Beer had said. He did not remember any case where the stone had formed after compression of the ducts by tumors. He did remember at least one case in which there was occlusion of the common-duct by gall-stones with stones in the hepatic ducts.

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DR. HARLOW BROOKS, *President*.

DEMONSTRATION OF A CASE OF HYDATID CYSTS OF THE LIVER; A CASE OF ECLAMPSIA WITH RUPTURE OF THE DIAPHRAGM.

J. E. WELCH, M.D.

DR. J. E. WELCH demonstrated a case of hydatid cysts of the liver. The subject from whom the specimen was taken was a native of Switzerland, forty-nine years of age. It was not known how long he had been in this country. He had been admitted to Bellevue Hospital on March 6. The family history was negative except

that his brother had tuberculosis. He had been in the habit of drinking about five or six glasses of whiskey daily and as much beer, but was not a drunkard. His personal history showed that he had had none of the ordinary diseases of childhood. He had had pneumonia about ten years before and since that time had had a cough. Eight years ago he had an attack of rheumatism which was repeated the following year. For five months before admission he had been coughing constantly and raising mucopurulent sputum which was never blood tinged. Three days before admission he had a sudden sharp pain in the right axillary region, followed by chilly sensations, but no distinct chill. Physical examination showed a well developed, fairly well nourished man. The action of the heart was weak. There were no murmurs. The right chest showed hydropneumothorax. The urine had a specific gravity of 1.024 and was negative. The sputum contained many tubercle bacilli. The temperature ranged from 98° to 103° for the first two days; on the following three days, which included the day of death, it ranged from 96° to 101° . The pulse ran from 96 to 140. At autopsy the right pleural cavity contained two liters of purulent fluid and air. The right lung was compressed to a mass about the size of the hand. The left lung was consolidated and contained many small tubercular cavities. There was general congestion throughout the abdominal organs. The left lobe of the liver was represented by a narrow margin of shrivelled tissue. Sections showed that the right lobe was congested and fatty. In the left lobe there was a cavity, eight cm. in diameter, having a thick fibrous wall, which contained a large echinococcus cyst. The cyst wall was folded upon itself on account of the confined space. There was no fluid present. No scolices were

found. The diagnosis was made by the outer laminated and inner granular layers of the wall as seen under the microscope. The liver and a portion of the cyst wall were exhibited.

DR. WELCH also reported a case of eclampsia with rupture of the diaphragm and stomach. No details of the clinical history were given. The patient was a woman twenty years of age. She was delivered at the hospital and two or three days after was taken with eclamptic seizure. She had several seizures one after the other in rapid succession for two or three days, and finally died in a convulsion. At autopsy the body showed a slight diffuse jaundice. The epicardium had several small punctate hemorrhages. There were small hemorrhages in both lungs. The liver was slightly increased in size and yellow in color. All the other organs were congested. Sections of the liver showed yellow areas, some fused, but for the most part the markings were irregular streaks of yellow. The central veins were somewhat dilated. There was general disintegration of the liver cells. In the cells were large deposits of fat, some in the shape of large globules. The kidney showed extensive parenchymatous change. There were two ruptures of the diaphragm on the right side, one around the left margin of the oesophagus, which admitted the passage of three fingers, the other about two inches to the left of the oesophagus. Here the muscle fibers were separated so far as to admit the passage of three fingers. The stomach was ruptured in three places along the lesser curvature and the contents had been forced through the diaphragm. There were about 500 c.c. in the left pleural cavity and 200 c.c. about the spleen. The contents were sterile, contained blood, and gave an acid reaction. The rupture was evidently very

recent as there was no inflammatory reaction in the peritoneum or pleura. Sections of the liver and kidneys were shown.

Discussion.

DR. HARLOW BROOKS said that so far as he knew this was the first case reported in this country of rupture of the diaphragm from eclampsia. He had been led to believe that it was very rare.

A CASE OF PRONOUNCED GENERAL OSTEOPOROSIS.

E. S. McSWEENY, M.D.

DR. E. S. McSWEENY reported a case of osteoporosis. The entire skeleton was exhibited. It was that of a fairly well nourished woman, forty years of age, five feet seven inches tall. Its weight was about seven pounds. The bones had first attracted attention in the dissecting room two months after death so that there was no record of their more recent state nor could any history of the case be obtained other than that the patient had died of pneumonia. Some of the vertebræ being the merest shells of compact bone tissue were almost completely destroyed in handling. As a whole the skeleton showed very little change in gross outline except a moderate cervico-dorsal kyphosis. There were no fractures, ankyloses, or similar lesions. The individual bones without exception showed very considerable loss of substance, chiefly of the cancellous tissue. The compact tissue was defective here and there, evidently from an extension of the process. The skull vault was almost sieve like; the scapulæ hardly

thicker than heavy paper and extraordinarily translucent; while in the long bones the shafts were chiefly affected. On looking over the very meager literature bearing on such conditions Dr. McSweeney had found but few cases reported. In these the changes were mostly local and not so extensive as seen in the specimen shown. As a general process osteoporosis was evidently rare and usually ascribed to senility or osteomalacia. The skeleton exhibited showed none of the characteristic senile changes and the age of the woman excluded such a possibility. Distortions of the bone were more characteristic of osteomalacia than of osteoporosis, whereas, in the present instance the reverse was true. The case was interesting surgically in that so extensive a lesion could exist in a woman of this class without the occurrence of a single fracture and with so little deformity. She had probably had to make her own living and, judging from the fact that she had been committed to the workhouse had led a rather hard life.

Discussion.

DR. P. W. NATHAN said that it was difficult to say much about the case since there was no history. The condition of the ribs and the spine and the condition of the neck of one femur reminded one of cases of osteomalacia. There had been cases of osteomalacia reported where the disease came on very suddenly and might involve the skeleton like this in a short time. Osteoporosis is not a disease as such; it is associated with many disorders of the bones. In this case he believed that the bones were probably soft in their original condition. Naturally after all the soft parts were removed they appeared much more brittle than they were during life. In osteomalacia there is always osteoporosis if the new

formed non-calcified osteal tissue is removed as was done in the present instance. He considered this a case of osteomalacia of some kind. The femur particularly was interesting.

DR. HARLOW BROOKS said that he was much interested in osteomalacia at present as he had been studying the disease in the primates where it was very frequently found. He had never seen anything which approximated the changes in these bones. He had not seen a condition of the skull such as was found here even in the fragile bones of the monkey. The condition of the thorax looked exactly like osteomalacia.

DR. NATHAN said that he thought the disease as found in monkeys was not exactly analogous to the osteomalacia found in man. It was more analogous to rickets.

DR. BROOKS stated that osteomalacia and rickets in the primates are two distinct and easily differentiated diseases.

THE ADDITION OF MARBLE OR OTHER CALCIUM COMPOUNDS TO NUTRIENT BROTH; A RELIABLE AND CONVENIENT METHOD FOR GROWING THE PNEUMO- COCCUS.

CHARLES BOLDUAN, M.D.

DR. CHARLES BOLDUAN demonstrated cultures of the pneumococcus growing in marble broth. During the course of his work with the pneumococcus he had felt the need for a fluid medium like plain broth in which there would be no body fluids. Plain broth was almost worthless, for growth seldom lasted for more than one or two

generations. He had at first tried to neutralize the broth to phenolphthalein but had found that did not work. The addition of glucose to the broth did cause luxuriant growth of the pneumococcus but the production of acid was so great that the cultures died off quickly. Attempts were then made to neutralize the acid formed by the addition of calcium carbonate. Experiments were made with glucose broth with calcium carbonate and with plain broth with calcium carbonate. The glucose broth proved to be unreliable, but the plain broth with calcium carbonate gave a good growth every day. In testing the acid in the various media it was found that cultures in plain broth with calcium carbonate usually remained neutral to phenolphthalein. He had at first thought that the calcium carbonate had neutralized the acids and that this was the reason for the luxuriant growth. It was, however, found that the cultures in the medium containing glucose died off very quickly and that the presence of calcium carbonate did not increase the viability. In plain broth cultures with calcium carbonate alone, the cultures in one case were still alive at the end of thirty days. When plain broth was inoculated there was often not only no increase but a positive decrease of organisms, whereas, when calcium carbonate was present there was a growth from the start. This fact could not be reconciled with the assumption that the calcium carbonate acts only by neutralizing the acids formed. Tests had therefore been made with other calcium salts, chloride and sulphate. These indicated that it was the calcium element, in part at least, which made the pneumococcus grow in this broth. Cultures of the pneumococcus grown in this broth lost little or none of their virulence. In preparing the marble broth the marble was broken into small pieces, then washed and put in

test tubes. The tubes were filled in the usual way and sterilized. The cultures remained viable full as long as ascitic broth cultures. The growth was not quite so profuse as in ascitic broth but was a marked growth. In the cases in which marble broth can be employed, its use obviates the tedious collection of ascitic fluid and the careful Pasteurization which ascitic broth requires.

Discussion.

DR. F. C. WOOD said that he had been much interested in Dr. Bolduan's remarks on the use of calcium carbonate. It had been employed by Dr. Hiss for a year and a half in keeping his cultures alive for a long time. Dr. Hiss had found it important to see that the pneumococcus flasks were shaken up every day. This brought the acid into contact with the calcium carbonate.

DR. BOLDUAN said that the point was not the neutralization of the acid, because when glucose was present the cultures die out as fast as without the calcium carbonate. The important point was that the pneumococcus needed the calcium salt in some form or other.

THE MACROSCOPIC IDENTIFICATION OF COLONIES OF THE PNEUMOCOCCUS.

LEO BUERGER, M.D.

The colonies of the pneumococcus when cultivated on the surface of certain solid media often present characteristics which are distinctive and diagnostic. These are made apparent when serum-agar or glucose-serum-agar is employed for the cultures.

The method of making up these media may be briefly described as follows. Neutral agar (to phenolphthalein) prepared preferably from meat infusion, and containing 1.5 to 2% peptone, and 2.5% agar, is melted down in large tubes. When it has cooled sufficiently (*i.e.* below the coagulating point of the serum to be employed), one third its volume of rich sterile ascitic fluid is added, the two are mixed and poured either into tubes or plates. Similarly, for the glucose-serum-agar, .5% to 2% glucose agar is used.

Although the appearances to be described are to be found on both of these media, that containing sugar is as a rule to be preferred. After eighteen to twenty hours, surface colonies of the pneumococcus show a circular disc-like flattened growth with a regular contour. When viewed from above the surface appears glassy with often a slightly depressed center. When looked at from the side, or by transmitted light they appear as distinct milky *rings* enclosing a transparent center. This form may be designated as the "ring type" of colony.

The ring colonies may vary considerably in their size as also in the finer details of their constitution. Thus the presence of rings can be detected in colonies which are scarcely larger than the period employed in ordinary newspaper type. Very large forms are occasionally met with after 48 hours cultivation. The largest I have seen measured 1.5 to 2 m.m. in diameter.

Often the characteristic appearance is not observed until 48 hours have elapsed. Such colonies are slightly convex at the end of 24 hours; if the plates be then allowed to stand at room temperature or be incubated for twenty-four hours longer, the typical form may develop.

The distinctness of the ring or raised periphery,

depends upon the opacity of the growth itself and upon the degree of umbilication of the center. Thus the glassy almost transparent looking colonies develop a fairly good contrast between periphery and center. After 24 to 48 hours their centers are practically transparent, and their peripheries, although not very markedly raised, appear as plain milky rings by transmitted light. When such colonies get old (72 hours or more) the opacity of their centers increases and the ring picture is less marked. The more opaque, denser growing, and whiter colonies have a decidedly elevated periphery. Their centers may, however, show more growth and be less transparent than those just described. But even this type often presents easily recognizable ring forms. The pneumococcus does not always present this appearance on the surface of the media recommended. At times attenuated forms grow in colonies too small for the recognition of distinct rings. Again, the convex type, and the large mucoid colony is to be found. When recently isolated from human beings or animals on favorable culture media, many strains, however, show this peculiarity. The persistence with which the ring-form clings to pneumococci which have been transplanted for many generations, varies considerably. I have found it four months after the isolation of the organism.

As far as I have been able to determine it is diagnostic of the pneumococcus. It must be differentiated from two other types of colonies; first from colonies with a prominent periphery (ring) occasionally met with in the case of streptococci, and secondly from those which show rings only by transmitted artificial light. The former, if carefully examined, will be seen to possess a distinct nucleus. This is never found in the characteristic pneumococcus form. The latter is not to be mis-

taken if it be studied by reflected light. Its centre is definitely raised above the periphery. When held up against an artificial source of light, such as an incandescent bulb, it appears to have a bluish peripheral ring. Such colonies belong to certain streptococci.

Finally it may be noted that in most instances this peculiar "ring-type" of colony is an expression of fairly luxuriant growth of the organism. In it the typical lanceolate encapsulated forms can readily be demonstrated.

CASES OF MYCOTIC ANEURISMS.

E. LIBMAN, M.D.

It is not my purpose this evening to go fully into the question of the pathology and causation of mycotic aneurisms nor to give full descriptions of the cases which we have seen at the Mount Sinai Hospital during the past four years. Before giving my brief sketch of the cases, however, I should like to mention a few points concerning aneurisms of this class, in doing which I shall follow closely the conclusions in Eppinger's paper on aneurisms.

In mycotic or parasitic disease of the valves of the heart mycotic emboli may be thrown off and be caught in arteries, especially at their point of division. Such a mycosis is generally due to staphylococci or streptococci. Such an embolus or secondary thrombosis may occur when the valves show the remains only of a mycotic endocarditis. At the position of the embolic thrombosis there is first an exudative inflammation, then there is an acute periarteritis with destruction of the media, and the

elastica and intima burst. If there should be a rupture of all coats of the vessel hemorrhage occurs either into the surrounding tissue or into the adventitia. As a result of these lesions there is a bulging of the vessel and in the wall of the dilatation all layers of the arterial wall are to be found. Such a condition must be considered an aneurism. These aneurisms are characterized by their multiplicity.

At the entrance to the aneurism the intima and the elastica are cut short; the ends of the latter are curled in indicating that there has been a tear; this tear is the mechanical explanation of the aneurism. The muscularis in some cases is torn at the entrance to the aneurism. This may be partial or complete. The adventitia also takes part in the formation of the wall and at times is the only part of the wall left in the aneurismal sac proper.

Eppinger further goes into the question of what changes occur when the aneurisms become chronic. He also points out the manner in which such aneurisms may become larger due to recrudescence, acute periarterial or mesarterial inflammations. Similar aneurisms, as is well known, can be produced by the presence of an animal parasite and occur in the mesenteric artery of horses where they are produced by a parasite—the *strongylus armatus*.

In *Albutt's System of Medicine*, in the article by Welch on "Embolism" there will be found a complete description of this condition and the complete literature. Welch draws attention to the fact that such aneurisms generally correspond to the point of lodgment of the embolus and are not situated proximally to it.

Osler reported in 1885 a very remarkable case in which there was an acute endocarditis and on the arch of the aorta there were four aneurisms. Three were small,

not larger than cherries and one was of the size of a billiard ball. The small ones were not noticeable as aneurisms from the inside but looked like fungous vegetations on separating which little slits could be seen leading to a saccular dilatation of the middle and outer coats. The large aneurism was thin walled and at its end and over the whole lining membrane of the sac there were many greyish green vegetations, some of which had perforated the sac and caused the rupture into the pericardium. Osler presumed that the ulceration had led to the aneurisms in the smaller sacs and the larger one he looked upon as a unique instance of a mycotic endarteritis.

This case of Osler's and a few other observations* have made it seem probable that mycotic aneurisms are not always to be explained in the way described by Eppinger, although in the larger number the explanation given by him seems to be the correct one.

The cases which I wish to present to-night are briefly as follows: (For the histories of the first two I am indebted to Dr. Joseph Wiener and for that of the third to Dr. Rudisch. There was a fourth case in the hospital several years ago in the service of Dr. Manges but this case left the hospital and the further course of the disease is unknown).

Case I.—W. W., 53 years of age, admitted October 8, 1900, to the service of Dr. J. Wiener. This patient took sick about a year previous to admission with chills, fever and sweating which occurred every two days and lasted about half an hour in all. After two weeks he was well for a time and then began to have the same symptoms over again until about a month ago. Since

* Of particular interest in this connection are cases of acute vegetative endarteritis of the open ductus arteriosus and a case described by Holst of aortitis with two aneurisms due to gonorrheal infection.

that time he has been having a feeling of weight in the epigastrium after eating, and pains radiating to the back and between the shoulders. His appetite was good. He lost 40 pounds in the last few weeks. Temperature on admission 99.6; urine negative.

Physical examination: General condition cachectic; slight icterus; thickening of the arteries. At the apex is a systolic murmur transmitted to the left; it is also heard over the arch and lower third of the sternum; the heart is enlarged both to the left and to the right. Examination of the stomach and abdomen reveals nothing except an indistinct small mass felt just to the left and below the umbilicus.

On October 11th the temperature rose to 103. Examination by test meal proved negative.

October 12th: Hemoglobin 33%; leucocytes 25,000.

October 13th: Exploratory laparotomy by Dr. J. Wiener. Exploratory aspiration was first performed in the splenic region and some clear serum was obtained on the left side at a depth of about three inches. Median laparotomy was then performed and the mass which had been felt was found to be a small aneurismal sac lying in the mesentery near the root. The subsequent history is unimportant except for the occurrence of some hemoptyses.

On October 28th there was marked twitching of the right hand and the patient immediately became unconscious and died early on the morning of the 29th.

At the post-mortem examination there was found a marked hypertrophy and dilatation of the left ventricle, atheroma of the mitral valve with ulceration and recent vegetations; there were 2 aneurismal pouches on the edge of the flap. The posterior flap showed some fine vegetations. The arch of the aorta was dilated and

showed marked atheroma. At the hilus of the spleen was found an aneurism of the splenic artery measuring about 6 c.m. in diameter; just below there was a sacculatation of about 60 c.c. The kidneys showed marked chronic interstitial nephritis. In the mesentery there were found two well-established aneurisms, one small area of ulceration and two developing aneurisms. Both the ulcerated areas and the well-established aneurisms showed distinctly the sharp break in the intima and the tendency to localization at the bifurcation of the vessels. These lesions were all situated in the branches of the superior mesenteric artery which supply the small intestine.

The bacteriologic examination of this case showed the presence of streptococci in the lesions.

Case II.—May C., 25 years of age, admitted April 13th, 1901. The previous history is negative. The present history is that 6 weeks before admission the patient took cold, had cough and mucous expectoration. She had tonsillitis at the same time; this lasted about two weeks. As the cough was getting better she noticed pain in the left groin on coughing and several small nodules were felt there. Three weeks before admission the patient noticed an increase in the swelling in the left groin which then began to pulsate; there was much pain present.

On admission there was found a loud, blowing systolic murmur at the apex of the heart which was heard in the axilla and posteriorly; second pulmonic sound accentuated. In the left femoral region there was an oval, elastic swelling about the size of a small bean; the tumor was painful to the touch, had expansile pulsation, and over it there was heard a loud systolic diastolic humming murmur with systolic accentuation. A diagnosis was made

of arteriovenous aneurism and the patient operated upon on the day of admission by Dr. Wiener.

The external iliac artery was tied in two places and cut between the ligatures; with the intention of tying the femoral artery below the sac. Resection of the lower end of the sac was attempted, but the blunt edge of the knife perforated the sac and profuse hemorrhage resulted which was controlled with considerable difficulty; finally, however, the femoral vein and artery were tied and all bleeding ceased.

The pulse and temperature rose after the operation and the patient complained of great pain in the left leg. Sensation was absent in the toes. During the night of April 14th the pulse became much poorer. It became stronger temporarily but the patient died on the following day.

At the autopsy the mitral valve was found thickened; the aortic flaps insufficient; on the under surface of one of the aortic flaps there were very large vegetations; on the center of this flap and at the margins of the other flaps were fine vegetations. There was marked atheroma of the aortic arch. The kidneys showed chronic interstitial nephritis; there was a small aneurism on one of the lesser branches of the renal artery. The intestinal vessels showed no changes. The external iliac artery was found divided and the ends ligated. The femoral artery showed quite marked endarteritic changes. There was an aneurism at the point where the profunda was given off. The sac contained thrombotic masses most of which were not at all decolorized. The remains of the vessel wall were present in the sac. The femoral vein had a small defect in its wall externally and anteriorly which led into the sac.

Bacteriological examination showed the presence of

staphylococcus aureus in the aneurismal sacs of the femoral and renal arteries. The heart blood showed streptococci and staphylococcus aureus.

Case III.—G. S., 24 years of age, was admitted to the service of Dr. Rudisch, September 18th, 1903. The history of this case is of much interest, but owing to its great length I can give but a few points here.

Previous history: Rheumatism in ankles and knees at the age of 9 and 14. No cardiac palpitation or dyspnea. The present illness is of 12 weeks' duration. For the first week of this time he had diarrhea. After this stopped he still felt poorly and was weak and had poor appetite. He had occasional cramp-like pains in the abdomen and also slight pain in the ankles and wrists. For 4 weeks his feet have been swollen whenever he was out of bed and for the past 4 or 5 days he has had cough. He still has slight fever at times and sweats a great deal at night.

Physical examination: Slight cyanosis; slight clubbing of the fingers; Lungs negative. Heart: Apex beat visible and palpable in the fourth space, one finger inside of the nipple. At the apex is a short systolic thrill and a short systolic murmur transmitted to the anterior axillary line, also the pulmonic area. The first heart sound is very sharp and the second pulmonic sound accentuated. No phenomena about the joints. Leucocytes 12,400; hemoglobin 50%.

September 23rd: The temperature which was 102° on admission ranges between 99 and 101. Urine is acid; shows a trace of albumin and some hyaline granular casts, also a few red and white blood corpuscles. There are petechial spots on the conjunctiva, palm of the left hand and on the cheeks. The diagnosis was made of mitral stenosis and acute endocarditis. The differential

blood count shows $76\frac{1}{2}\%$ polynuclears, 22% lymphocytes and $1\frac{1}{2}\%$ eosinophiles.

October 4th: There are new petechiæ. Treatment by injections of collargol.

October 19th: At the junction of the upper and middle third of the right thigh just to the outer side of the femoral artery is an elongated bulging mass $1\frac{1}{2}$ inch long which runs parallel to the femoral artery and is slightly tender. It does not seem to pulsate and does not disappear when the artery is occluded.

October 21st: Bruit and expansile pulsation detected in the swelling in the femoral region. The diagnosis is made of the presence of a mycotic aneurism.

October 26th: The mass has increased and is distinctly cystic; seems to be attached to the bone.

October 28th: Acute parotitis on the left side.

October 29th: On aspiration of the mass in the right thigh pure blood is obtained.

October 31st: Attack of right hemiplegia with absolute aphasia; during the day gradual partial return of speech.

November 2nd: Marked motor aphasia. Diagnosis made of probable rupture of mycotic aneurism of one of the branches of the left Sylvian artery.

November 3rd: Parotitis has disappeared.

November 16th: Heart dullness extends $4\frac{1}{2}$ c.m. to the right of the middle of the sternum.

November 29th: Operation performed by Dr. Lilienthal. An incision was made over the elastic swelling which was found to consist of a softening laminated blood clot. The lateral aspect of the femur had been eroded for about 2 inches of its length and to a depth of about $\frac{3}{8}$ of an inch and the walls of the defect were quite

rough. The clot was removed and the cavity firmly packed.

December 14th: Hemorrhage from aneurismal sac controlled by packing.

December 26th: Femoral artery tied by Dr. Lilienthal, the bleeding having been found to come from a small rupture in the wall of the artery.

January 1st, 1904. Sudden rise of temperature to 103.8; evidences of pneumonia on the right side of the chest. The patient died on the evening of the same day.

During the stay of this patient in the hospital his temperature occasionally rose to 102°, 103° and 104° but generally only for one day at a time. During long periods it ranged between 97 and 101 and even 99 to 100. Pulse ranged between 80 and 100 but later rose to 120. White blood count varied between 10,000 and 15,000. Collargol seemed to have no effect upon the course of the disease.

Bacteriological examination. On September 23rd, September 30th, October 23rd and November 2nd, blood cultures showed the presence of a small number of attenuated streptococci which were possessed of moderate hemolytic power. At the time of the operation upon the aneurism in the thigh cultures were made from the laminated clot and streptococci found.

At the post-mortem examination there were found pneumonic areas in both lower lobes of the lungs. The heart showed hypertrophy of the left ventricle and dilatation and hypertrophy of the right auricle and ventricle. The mitral valve showed a moderate stenosis. There were bright yellowish green vegetations on the flaps and on the surface of the auricle. There were small, yellow infarcted areas in the heart wall but no emboli were

found in the branches of the coronary artery. The spleen, which was enlarged was deformed by recent and old infarcts. The infarcts in the spleen were of the striking yellowish color which we have repeatedly found in splenic and renal infarcts in cases of acute endocarditis due to attenuated diplococci and streptococci. The kidney showed recent and old infarcts. On the branches of the superior mesenteric artery there were several aneurisms, two of these being about the size of a walnut and the other two about the size of a bean. The liver was very large, congested, fatty, and there was a large aneurism at the hilus developed from the right branch of the hepatic artery. Near the surface of the liver were numerous small, irregular yellowish areas. Part of the right femur was removed. It showed marked erosion. The exact origin of the aneurism could not be traced as the aneurism had been opened up during life and the sac at the post-mortem examination was found almost entirely destroyed by suppuration.

Bacteriological examination showed the presence of the same attenuated streptococci in all the organs that had been present during life.

There are a few other points to which I should like to draw special attention.

In the second case we have to do with an arterio-venous aneurism of the femoral artery, apparently secondary to a tonsillitis. In the third case the rapidity with which the femur was eroded was certainly very striking. It will also be noted that in all three of the cases there was present a chronic interstitial nephritis. It is likely that this predisposed to a general infection and made both the valves and the vessels more liable to being attacked by the bacteria.

Addendum.

I append here the important papers recorded since the publication of Welch's monograph.

- Holst, *Norsk Magazin for Lægevidenskaben*, No. 4, 1901. Reviewed in *Deut. med. Woch.*, Litteratur-Beilage 1901, p. 107.
Simonds, *Deut. med. Woch.*, 1901, p. 353.
Ling, Reviewed in *Lancet*, June 29, 1901, p. 1846.
Duckworth, *Medical Press and Circular*, June 12, 1901.
Canon, *Mittheilungen aus den Grenzgebieten*, Vol. X, p. 419.
Gabriel, *Wien. klin. Woch.*, 1901, p. 1051.
Huchard and Bergougnian, *Journal des praticiens*, Jan. 4, 1902.
Galavardin, *Cent. f. innere Medizin*, 1902, p. 293.
Brion, *Deut. Aerzte-Zeitung*, 1901, No. 18.

Discussion.

DR. JAMES EWING said that he had been greatly impressed by the extent of the aneurisms in these cases. When Dr. Libman had called attention to the fact that the patient in the second case had had an attack of acute tonsillitis six weeks before death, he had received the impression that Dr. Libman intended to connect the tonsillitis with the development of the aneurisms. The examination showed that the heart valves and aorta exhibited old lesions favorable to the development of aneurisms so that it would seem difficult to demonstrate that these aneurisms developed as a sort of sequela to the tonsillitis.

DR. LIBMAN said that prior to the attack of tonsillitis this patient might have had fever. Of this, however, there was no evidence. But he thought it was not at all improbable that there was a connection between the aneurism and the tonsillitis. It is a clinical fact that tonsillitis predisposes to systemic infection with the production of acute endocarditis, acute nephritis, and other lesions. It would not take long for thrombotic masses or vegetations to form on valves already the seat of disease and the lodgment of such emboli from such sources

in vessels could readily produce mycotic aneurisms. It was remarkable how rapidly such aneurisms could be formed and how readily they could rupture or invade the surrounding tissues.

SOME OBSERVATIONS ON THE SUBWAY AIR.

E. E. SMITH, M.D.

DR. E. E. SMITH presented some observations on the air in the Subway which he had made in the month of December at the request of the Health Commissioner. They were few in number but were systematic and were believed to show some general conditions. The air was taken from the cars of the Subway during operation, and, for comparison, from the Subway stations and from cars of the elevated road, and from the outside atmosphere at a distance of five feet from the level of the street. The temperature and humidity, the amount of oxygen and carbon dioxide, and the number of micro-organisms in the air were studied. The results did not afford any basis for adverse criticisms. The figures obtained were as follows:—

Date	Source	Temp F.	Relative Humidity (approx.) %	Oxygen %	Carbon dioxide Pts. in 10,000	Micro-organisms No. in 10 liters		
						Bact.	Moulds	Total
Dec. 6	Subway car, empty.	57°	58	20.6	7.0	103	110	213
6	" " full ...	57°	66	20.7	8.1	113	120	233
15	" " few ...	53°	59	20.6	6.9	101	97	198
16	" " few ...	58°	53	20.3	5.0	67	49	116
16	Subway station.....	54°	60	20.8	5.5	60	83	143
16	" "	55°	60	20.7	7.0	151	104	255
16	Elevated car, empty	55°	50	20.7	5.9	17	10	27
16	" " full...	50°	58	20.7	8.5	11	53	64
6	Street, no wind.....	35°	—	20.7	3.4	11	4	15
15	" " snow	25°	—	20.6	4.4	15	2	17
16	" " "	32°	—	20.8	3.8	16	6	22

The temperature and humidity did not indicate conditions to cause discomfort. The amount of oxygen of the air was found to be normal. An indication as to whether air is vitiated is found in the amount of carbon dioxide present. Pure air is put at 3 to 4 parts in 10,000. Authorities agree that 7 parts in 10,000 is the upper limit of safety. In this respect the air in the Subway cars is not worse than the air in the Elevated cars. Bearing in mind the temporary occupancy of the cars the carbon dioxide did not show an alarming percentage. The air in the empty or partially filled cars was within the safety limits. In regard to the number of micro-organisms found under present conditions, there was one striking fact, namely, the large proportion of moulds present. After considering the possible causes Dr. Smith believed that two might very probably exist:—first, that the atmospheric conditions, the absence of light and the moisture of the walls, owing to their being recently built, were favorable to the development of moulds; second, that the production of currents of air by the movement of the trains kept the moulds in suspension in the air. The constant moving of the air tended to prevent their settling out. The question of the influence of the presence of moulds on health was one on which our present knowledge is too meager to permit of definite conclusions.

Discussion.

DR. JAMES EWING said that he was much interested in these figures, which, as he understood them, indicated a very much larger bacterial and mould content in the Subway air than in that of the street. He had not understood exactly how these tests were made on the street, but it seemed at any rate that it would be a dangerous thing to go into the Subway if there were so many more

micro-organisms in the Subway than there were in the street. Some years ago he had made some tests on the bacterial condition of the air of the streets for Dr. Woodbury. They were intended to determine how many bacteria would fall on Petri dishes exposed in various places. There was an enormous difference in the number of bacteria in the air of different streets and in different states of weather. It seemed to him that unless these experiments were very carefully controlled as to temperature, air currents, etc., they were unfair as a comparison between the air of the street and that of the Subway.

DR. SMITH said that Dr. Ewing's remark especially applied to observations made with Petri dishes and not to the same extent to air examined by passing through the aërobiscope where the surface was not exposed in that way. The air had been taken at five feet above the surface of the street, and it was taken in a spot where it was guarded from wind. On one or two occasions there was snow on the ground so that there could have been but very little dust. The temperature in the street was 25° to 35° F. Dr. Smith did not think that the figures given were in any way alarming. They were no greater than were found in crowded rooms in our own houses. Personally he believed it quite possible that the growth of the moulds was very largely due to the damp condition of the Subway when it was first opened. He would not be at all surprised if later observations should show that the growth of the moulds had become very much less.

REPORT ON SOME OBSERVATIONS ON FATTY EXTRACTS FROM ORGANS.

E. K. DUNHAM, M.D.

DR. E. K. DUNHAM reported some observations on fatty extracts from organs. He had been working on the extracts, from kidneys especially, for a year or two, his attention having been called to the subject by a question which came into his mind as to whether the fatty changes which are so familiar were really due altogether to the presence of neutral fat. He had speedily come to the conclusion that what was usually regarded as fat was really not only neutral fats, but contained, in addition to this, a very considerable amount of other fat-like substances, among them lecithin and protagon. Quantitative analyses of these substances had been made with some degree of success and it had been found that in fatty extracts from the kidney the amount of lecithin ranged from about 30 to 67 per cent. of the extract; showing that there might be as much or more lecithin or phosphorized fat as neutral fat in these organs. His reasons for using the kidney were, in the first place, because the kidney was easily freed from obvious fat; secondly, because it hardly seemed probable that the kidney could be regarded as in any sense a normal fat depot. This was certainly not true of the liver. The results of examination of the liver varied somewhat from those of the kidney. One or two other organs had been examined in a less thorough way. The fact that these phosphorized fats were so uniformly present in the cells and were really so abundant, making up something like 6 to 8 per cent., in one case 10 per cent., of the total solids of the organ, suggested that they were very important cell constituents, and furthermore suggested that

possibly some of the fat found in the different forms of degeneration might be in part lecithin or phosphorized fat, in part a neutral fat derived from the fatty acids they contained since the fatty acids might be split off from these phosphorized fats. It was interesting in this connection to recall some observations made by Albrecht, published in the Transactions of the German Pathological Society, in which he calls attention to the fact that there are certain minute structures in cells which are double refracting. That was true in the case of both protagons and lecithins. These are double refracting substances. Albrecht called attention to the fact that these fine granules ("liposomes") occur in the heart in a series of rows lying between the longitudinal striations of the muscle fibers, and also to the fact that the fatty granules first appear in this situation in fatty changes in the heart. He is inclined to think that substances like protagons may become modified in such a way as to give rise to these fat droplets. There was one very extraordinary physical quality of these phosphorized fats and that was their power of taking up water and producing myelin forms so that a mere trace of lecithin put on a slide and moistened would make a hundredfold its bulk of myelin figures. It seemed to absorb water and swell up with interesting and curious motions, growing so fast that one could watch its development. It had been suggested that these phosphorized fats and lecithin-like bodies or lecithins might be a very important constituent in cytoplasm in causing the other constituents to assume and maintain the form of an emulsion in which the bodies in solution are separated into droplets by a film of myelin substance very sensitive to variations in the amount of moisture. Perhaps the changes which are known as parenchymatous or fatty degenerative changes might have to do with

modifications in this emulsion in which these myelin films may form essential parts. Possibly in the minor degrees of these changes we may have more imbibition of water through osmotic pressure. In the more chronic fatty changes it is possible that we have a chemical change in the myelin substance. It was pretty certain that a complicated molecule like these lecithins, present in the cell in such abundance, must be of deep significance. So far as microchemical staining reactions go, the lecithins will take up those we are accustomed to use for neutral fats. It is more possible to make a distinction by means of polarized light. Many of these substances are double refracting, but it is exceedingly difficult to make very accurate observations respecting double refraction on minute fatty granules.

A NOTE ON A PECULIAR ACTION OF A STREPTOCOCCUS ON BLOOD PLATES.

E. LIBMAN, M.D.

It has been repeatedly noted in studying the growth of streptococci on plates of blood-agar that the streptococci vary as to their influence on the surrounding medium. Some will cause a disappearance of the blood in a larger or smaller area about the colony and some will not have any effect of this kind. Some authors are of the opinion that the hemolytic effect, so-called, varies in accordance with the virulence of the organism. This we have not found to hold. The streptococcus on the plates which I show you this evening was isolated by Dr. Bauman from the blood of a case of phlebitis and peri-

phlebitis of the leg. On the blood-agar plates it was noticed that after twenty-four hours the organism was surrounded by a clear area. Surrounding this clear area the blood on the plate was darker in color than on the rest of the plate. After forty-eight hours a second clear ring appeared outside of this area of darkened blood. In one observation the process extended so that there were three clear concentric rings about the streptococcus colony. It was very difficult to explain how the organism could produce a result like this.

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DR. HARLOW BROOKS, *President.*

A CASE OF PERNICIOUS ANEMIA WITH MEGALOBLASTIC CRISIS.

WILBUR WARD, M.D.

The following case of pernicious anemia is presented chiefly on account of the enormous numbers of nucleated red cells present in the blood, and the lesions in the spinal cord. The patient was an Englishwoman, 69 years of age, who was admitted to the service of Dr. V. H. Norrie, at St. Luke's Hospital, on February 28, 1905. Her family and past history showed nothing except that she had suffered from frequent attacks of acute articular rheumatism. Aside from minor complaints she had been in good health until nine months before admission when she began to experience numbness and tingling of the fingers and palms of the hands. Some weeks later the same sensations were felt in the feet, gradually extending up the legs and on to the inner surfaces of the thighs. Her hands and feet were continually cold. Towards the middle of winter she became physically weak, was unable to do her daily work as seamstress and began to develop dyspnœa. There was marked anorexia and occasional vomiting attacks and obstinate constipation. Three weeks before admission to the hospital the extreme weakness compelled her to go to bed, and swelling of the feet and legs was first noticed. The sensory disturbances in the extremities became very troublesome and she came to the hospital on February 28, complaining of the weakness and dyspnœa and coldness of hands and feet. Physical examination showed a woman of medium frame, fairly well nourished, but with very pale mucous membranes, and the characteristic sallow appearance of the skin, which alone led to the tentative diag-

nosis of pernicious anemia later confirmed by the blood examination.

The heart was slightly enlarged to the right and two distinct murmurs were heard, one, soft and blowing, systolic in time, heard best at apex and transmitted as far as the left mid-axillary line; the other, a loud systolic murmur at the aortic area, transmitted up to the neck. The pulse was regular, 120 to the minute, of fair size but of poor force. The lungs were negative, as were the liver, spleen, and kidneys. The urine was normal. The extremities showed marked œdema of the legs and feet.

Upon admission, the patient was given an iron tonic with Fowler's solution in increasing doses until M XV t. i. d. was being taken. For some days her condition remained the same; then the symptoms of anemia became aggravated, the dyspnœa and restlessness extreme, a distressing sense of constriction about the lower part of the chest and upper part of the abdomen constant, and after a few days of semi-consciousness she died on March 22.

Blood examinations were made at frequent intervals and with but few exceptions smears were obtained every day. These were stained by the Jenner method, this stain being used for routine work in the laboratory. The accompanying table shows partial results of such examinations. For most of the differential counts 500 leucocytes were counted, this being the case on all the days when the number of megaloblasts to the c.mm. was estimated. This latter was arrived at in the following manner. While counting the differential the number of nucleated red cells seen was noted. (This in the table is reduced to the number per 100 leucocytes). The total leucocyte count was then taken (Thoma-Zeiss) and the relative numbers of leucocytes and nucleated reds esti-

mated pro rata, inasmuch as all nucleated cells are counted in the usual leucocyte count.

An attempt was made to differentiate between megaloblasts and normoblasts, but was abandoned because owing to the gradation in size accuracy was impossible. The vast majority of all the nucleated cells, however, were true megaloblasts. On the later days, in fact, normoblasts were rarely seen. Aside from the great number of megaloblasts, the blood presented the picture commonly seen in pernicious anemia. The red cells ranged from 1,250,000 on admission to 1,040,000 on the day of death, and the hemoglobin dropped from 33 per cent. to 25 per cent. (Fleischl-Miescher), the color index being high (1.24) as is not unusual in severe cases. The average size of the red cells was much above normal, megalocytes being very abundant, some of them of extreme size, and most of them stained deeply with the eosin of the Jenner. Poikilocytosis was marked, all varieties of shapes being seen, and polychromatophilia was frequently observed in both nucleated and non-nucleated cells.

The leucocytes were low throughout, ranging from 5,180 to 3,250, and the usual lymphocytosis was present, the lymphocytes, mainly of the small variety, ranging from 38 to 46 per cent. Myelocytes were occasionally observed and on March 4, 3.5 per cent. of eosinophiles were present. No mast cells were seen at any time.

The chief interest in the case is the number of megaloblasts present. As seen from the chart on March 18 but five were seen while counting 500 leucocytes, and this number was increased until on the day of death, March 22, 1,503 were observed during the same count. With a leucocyte count of 13,000 on that day, the estimated total number of nucleated reds to the c.mm. was 9,750, while



FIG. I. Section from dorsal region of Cord.

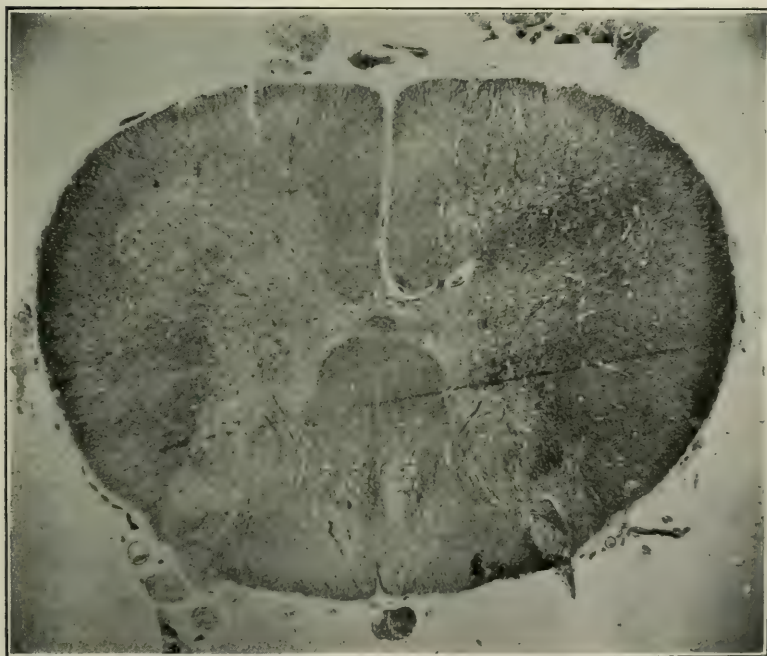


FIG. II. Section from lumbar region of Cord.

the estimated actual number of leucocytes was 3,250. This count of 9,750 to the c.mm. exceeds considerably the highest count I have been able to find in the literature. Cabot reports one of 7,100. The rise in the number of nucleated cells was for the most part gradual, but a sharp increase probably took place on the 19th, the number being more than double that on the 18th. The nuclei of the megaloblasts were for the most part of the small pycnotic type and not of the large variety with a well marked chromatin network occasionally seen. Mitoses were frequently seen but they did not appear to be as numerous as one would expect from the total number of megaloblasts.

All the other morphological changes in the red cells usually seen in the disease were much better marked towards the end than when the case first came under observation, as may be seen by comparing the smears made on March 1 with those made on March 22, which are under the microscope.

Autopsy.—All the serous cavities contained moderate amounts of fluid. The pericardium was coated with small patches of fresh fibrin, and while the heart was of normal size and appearance, the muscle was flabby but not so fatty as is usually seen. The valves, especially the mitral, showed old endocarditis, which caused a considerable degree of mitral insufficiency which undoubtedly contributed to the early death of the patient.

The liver was large, with a smooth capsule, and was moderately fatty. Sections stained by ammonium sulphide showed the presence of small amounts of iron, but no reaction was obtained by the use of potassium ferrocyanide and ferricyanide. The kidneys were of the atrophic granular type and showed the changes of a moderate degree of chronic diffuse nephritis. The stomach and

intestines were normal and careful search failed to reveal the presence of any parasites or ova.

The bone marrow was very red and hyperplastic and it filled the whole length of the medulla of the long bones. As may be seen from stained smears, great numbers of megaloblasts were present in addition to the elements usually found. Only an occasional mitotic figure was seen.

The spinal cord in the gross was apparently normal but sections showed moderate swelling and disintegration of the myelin of the nerve fibers, and an occasional small patch of focal sclerosis. These changes were small in extent in any one place and were not localized in any one segment or column of the cord. They corresponded closely to lesions of the cord described in pernicious anemia and are of interest as explaining the sensory disturbances of the extremities and the girdle sensations about the trunk, so often complained of by the patient during the last few days of her illness.

Changes in the blood vessels, such as have been noted by Minnich and Nonne, were not present, nor was there dilatation of the perivascular lymph spaces. It is important to remember that these lesions of the cord present in pernicious anemia are not specific for this disease. Redlich has shown that they may occur in diabetes, pellagra, and diphtheria, and also in cases of metallic poisoning. In experimental anemia produced by injecting hemolytic substances into animals, the cord has also shown the lesions described above. Von Noorden has described a case of pernicious anemia with marked lesions of the cord in which there was degeneration of the peripheral nerves chiefly of the tibial group. There were no clinical symptoms of the lesion. No such changes were found in the case above reported.

Date	Hgb.	Red Cells	Leuco- cytes	DIFFERENTIAL				Nucle- ated Reds	Estima'd number to the cubic mm	Estima'd actual Leuco- cytes
				Neut.	Lym.	Eosin.	Myel.			
March 1	33%	1,250,000	4,200	60	40	0	0	1		
March 4				56	40.5	3.5	0	4		
March 9				53	46	0	1	34		
March 11	32%	1,300,000		55.5	42.5	0	2	87		
March 12				58.5	39.5	1	1	67		
March 13	31%	1,232,000	8,300	59.5	38	2	.5	58	3,120	5,180
March 14				59	40	1	0	68		
March 15				61	39	0	0	61		
March 16				54	46	0	0	99		
March 17				59	41	0	0	99		
March 18	29%	1,096,000		58	42	0	0	95		
March 20			12,400	56	43.5	0	.5	198	8,236	4,154
March 21	27%	1,108,000	12,250	54.8	45.2	0	0	237	8,615	3,636
March 22	25%	1,040,000	13,000	57.8	41.4	.6	.2	300	9,750	3,250

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A CONGENITAL HEART LESION.

F. N. CHESSMAN, M.D.

The following case is that of a boy, twenty-two months old, who was admitted to St. Luke's Hospital, in the service of Dr. V. H. Norrie, with the diagnosis of sub-acute cerebrospinal meningitis. It is of especial interest on account of the congenital heart lesions present and from the fact that these lesions were diagnosed during life. The child was apparently perfectly well until forty days before admission, when he vomited at night, and the next day his mother noticed that his neck was stiff. The second day after; he had spots on his body which his mother thought were measles. For two weeks his condition was fair and he talked and played with toys. He then became worse. His mother noticed that his eyes were "turning" and he appeared "deaf" to her. Apparently this means that the child was unconscious. This condition persisted for two weeks, and the day before admission he had a convulsion for the first time.

On admission, his tongue was moist and coated. He had retraction of the head and rigidity and pain in the neck. There was a partial Kernig's sign with much pain. The eyes were fixed; and the pupils normal. The apex beat of the heart was just outside of the nipple line. Over the entire precordia there was a loud, harsh, blowing, systolic murmur heard with greatest intensity at the left border of the sternum at about the fourth space and sounding very close to the ear. On the left chest, above the precordia, there was a constant, blowing, humming murmur, intensified and of higher pitch during systole, and heard with greatest intensity just below the clavicle. This seemed to be distant from the ear. The

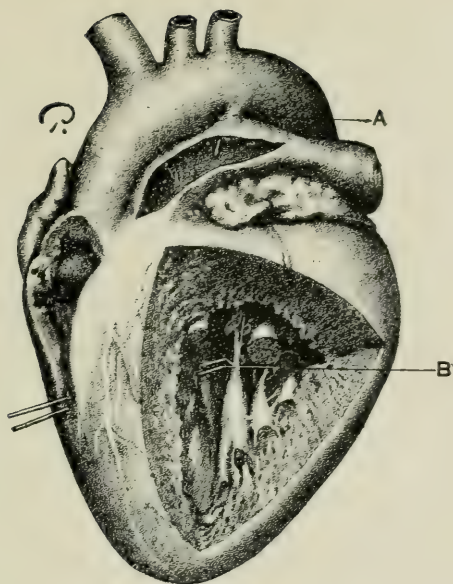


FIG. I.

- A.* The patent Ductus arteriosus.
B. Foramina in Ventricular septum.

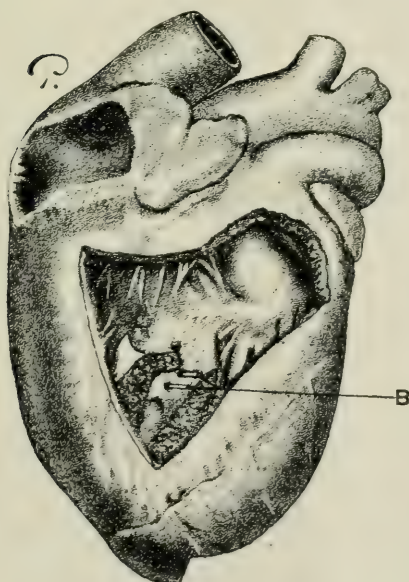


FIG. II.

View of right ventricle showing at *B* the openings in the ventricular septum.

child's pulse was regular and of fair size and force. His lungs were clear, his liver and abdomen normal. There was no clubbing of the fingers and no cyanosis.

On the day after admission a lumbar puncture was done and 10 c.c. of amber colored fluid was obtained. The diplococcus intracellularis was found.

For two weeks the condition of the child remained about the same; he never regained consciousness. The physical signs of the heart remained unchanged, and his pulse continued to be regular and of good force. He died suddenly on the fourteenth day after admission to the hospital.

At autopsy, the head was enlarged, the vertex prominent, and the opening of the anterior fontanel was small. *Brain.*—The dura was very adherent to the calvarium and under the pia of the vertex there was a great deal of exudate which was thick and dry in character, and did not look like fresh pus. There was also a great deal of exudate about the base of the brain. The convolutions of the brain were flattened and there was great dilatation of the lateral, third, and fourth ventricles which contained clear fluid. The brain substance was pale and œdematous, and there was little congestion of the tissue. The cord was covered with thick exudate. *Heart.*—Not enlarged; muscle normal. There was a patent ductus arteriosus with opening about two mm. in diameter. The length of the duct was about four mm. There were two openings in the ventricular septum, each about one mm. in diameter, and placed low down in the septum, instead of high up just beneath the semilunar valves, as is more frequently the case. The openings on the left side were twenty mm. above the apex and sloped downward into the right ventricle to a point only about ten mm. above the termination of the cavity. The foramen ovale was

not entirely closed but the opening was very small and was not greater than that found in many children of this age. The tricuspid, mitral, and both semilunar valves were normal. There was no stenosis of the pulmonary artery. The lungs were fully aerated and there was no pneumonia. The liver showed some congestion. The kidneys were somewhat congested. The spleen, pancreas, and suprarenals were normal. There was slight swelling of Peyer's patches and the solitary follicles in the intestines. The mesenteric nodes were much enlarged, but there was no evidence of tuberculosis. Cultures from the fluid in the ventricles and from the exudate did not show meningococci. Smears from the brain and cord showed no organisms.

Discussion.

DR. W. P. NORTHRUP said that the specimen had interested him very much. He had thought that he had learned that all children who survived to the age of twenty or twenty-four months, and had a harsh, purring murmur at the left margin of the second space, had one thing the matter with them; namely, narrowing of the pulmonary artery or orifice with incomplete closure of the septum ventriculorum. He had watched two children at the Foundling Hospital for several months. The clinical symptoms presented differed slightly. In one there was an area of dullness at the left side and high up toward the neck. At autopsy, however, both had the same condition; namely, narrowing of the orifice and incomplete septum. Both patients had a blue tinge and clubbed fingers. Another case had been seen in the Presbyterian Hospital, of a man thirty-five years of age. He was a little blue, but he had never known of any

trouble with his heart. He had been brought into the hospital comatose. There was this peculiar murmur at the left second space. At autopsy the man was found to have the same condition as the two children mentioned. The surprising thing was that these two cases in children had other diseases most trying to the heart. One had whooping-cough and pneumonia; both had measles and bronchitis. It was astonishing how these hearts lasted until they got ready to give up, whatever the temporary acute disease. Three cases reported had died of abscess of the brain. The man at the Presbyterian was among those who had had abscess of the brain. In the case here reported he noted that the walls of the right ventricle were not thickened and the patient was not a blue baby. The case seemed to be in a distinctly different class from any he had ever met. He had recently seen at the Presbyterian Hospital a young child who was blue but who did not have the characteristic murmur at the left margin. It might be like the case here presented. No autopsy was obtained. The case here differed from those Dr. Northrup had seen in not being cyanotic and in not having an enlarged right ventricle, but having the characteristic murmur.

DR. J. H. LARKIN said that it had been his fortune to see two adult hearts in which there was a hole through from the left into the right ventricle. One case had died of lobar pneumonia. He had never been blue and was a man of fine physique. There was no mention made in the clinical history of anything wrong with his heart action. The lumen in the heart was directly beneath the aortic valve. It was a very large opening and the edges were more or less cicatricial. The other case showed a similar hole, not quite so large, but situated in about the same position as the specimen shown. Dr. Larkin did

not think it was uncommon to find such lesions in individuals who were not blue. In these congenital lesions of the heart there was a possibility of the hole being closed up by the muscular action of the heart without any change in the arterial or venous blood.

DR. E. LIBMAN said that the lesion which lasted into adult life which was most likely to have a lack of cyanosis was an open ductus arteriosus. The diagnosis was not difficult if there were present a systolic-diastolic murmur in the pulmonary area. The accentuation of the second pulmonary sound was an important diagnostic point. If the second sound was not accentuated one must think of an open ductus arteriosus with a complicating lesion such as a stenosis of the pulmonary conus or an open septum ventriculorum.

CHORIONEPITHELIOMATOUS PROLIFERATIONS IN TERATOMA.

ROBERT T. FRANK, M.D.

The chorionepithelioma of the uterus is no longer considered an uncommon condition; more than two hundred cases have been reported. During the last few years several tumors which bear a striking resemblance to the chorionepithelioma of pregnancy have been found in the testicle. The identity and classification of these neoplasms has furnished a fruitful source of discussion.

In order to apply with propriety a term such as chorionepithelioma to tumors in which the age or sex of the patient vouches for a complete dissociation from pregnancy proof is required that these tumors arise from

vital processes, analogous to those of the formation of the embryo, and the evidence that the suspected tissue corresponds to the epithelial covering of the chorion in genesis, physiological and morphological characteristics.

The embryonal derivation of these tumors, as shown by their occurrence as an integral part of the teratoma, is not difficult to demonstrate; it is also possible to show a direct continuity of the suspected tissue with ectodermal structures, never with others (Pick, Risel). But by proving them a derivative of the ectoderm we still fail to establish their identity as an exact analogue of the chorionepithelioma.

We cannot hope to find such highly specific characteristics as those seen in the more completely differentiated tissues, such as, for instance, the presence of hair found in the epidermis of teratomata, or the nerve cells seen among the glia and brain tissues of embryoms; but yet there are more general and group-like qualities which are nearly as specific.

For comparison we must turn to the normal chorion as well as to those hydatid and chorionepitheliomatous tumors in which the connection with pregnancy is direct and evident. We are further limited to characteristics which leave some permanent trace and furnish a morphological picture, from which, however, physiological as well as purely morphological facts may often be deduced.

The normal trophoblast is composed of three cell forms—Langhans' cells, chorionic wandering cells, and syncytium—which proliferate rapidly, invade the maternal tissues, and especially the blood vessels, cause hemorrhages, necroses and fibrin formation, and having fulfilled their functions during gestation are cast out or absorbed. Similar cells appear in the malignant growths

of pregnancy, evince the same properties, often to a still higher degree, but fail to stop in their course. Once having entered the blood vessels rapid and fatal metastases occur, each metastasis faithfully copying the primary growth. Such tumors, whether they assume the typical or atypical form described by Marchand, are recognized and accepted when in direct connection with pregnancy, partly because of this relationship, partly because they so faithfully reproduce the normal trophoblast. Were we merely to attempt to analyze individual cells such analysis would prove as unfruitful as a similar analysis practiced upon the individual cells of a carcinoma or sarcoma.

Therefore, every attempt to prove that a teratoid tumor is or is not a chorionepithelioma which is based upon any single feature such as the size or configuration of a cell, or even upon a supposedly more specific feature, such as the presence or absence of syncytium, is foredoomed to failure. For this reason such arguments or facts as the following:—that syncytium is no specific structure because the uterine mucosa undergoes syncytial changes in ectopic gestation (Schmidt); or that syncytial masses are found in carcinomata and endotheliomata (Recklinghausen); or that syncytium may be imitated by undivided liver cells in adenocarcinoma gigantocellulare (Babes); or, finally, that the syncytia seen in material preserved in formalin-Müller are an artefact (Sternberg);—lose their weight.

Nevertheless, no authors, to my knowledge, have found typical syncytium with vacuolated, foamy appearance, ciliary margin, and vasodestructive qualities in any tumors except chorionepitheliomata.

My object to-night is to demonstrate several specimens of these growths, and also to present certain con-

clusions which I hope shortly to publish in a more extensive paper.

Of the three tumors which I have had the opportunity of examining, two are tumors of the testicle, which I have received through the kindness of Dr. F. C. Wood; the third is a supposedly primary tumor of the mediastinum from the collection of the Pathological Laboratory of the College of Physicians and Surgeons. All three are derived from males, in one only have I been able to find teratomatous constituents, and yet I am prepared to show that all three are chorionepithelioma. Such assertions should be based upon solid proof to carry any weight. Before attempting to offer this proof it will be necessary to give at least a brief outline of the material, sections of which are now under the microscope.

CASE I. The patient was a young adult, twenty-one years of age, who presented the symptoms of an intrathoracic tumor, first diagnosed as an aortic aneurism, but later recognized as a malignant growth. The testes were not examined at autopsy, and presumably were not enlarged. No record of the autopsy was kept, but from personal inquiry I have found that no dermoid of the mediastinum was noted. But little of the material from the supposedly primary mediastinal tumor was preserved. Several hemorrhagic nodules from the liver and lungs, beside two liver nodules of lighter color and different appearance remained.

The metastases are circular, hemorrhagic, their center necrotic, at the periphery are epithelioid cells, large plasmodial masses, transition types, hemorrhages, and fibrin. No connection with either liver or lung tissue could be demonstrated. In the surrounding liver cells large quantities of bile pigment occur, but nowhere is it seen within the tumor cells. The two whitish metas-

tases are not hemorrhagic, and are traversed by connective tissue bands. Microscopically a large, alveolar structure, composed of epithelial cells of uniform size and shape, is revealed.

CASE II. This case is that of a large tumor of the testicle from a man of forty years, operatively removed; the subsequent history is unknown. This tumor shows extensive necroses and hemorrhages. Teratomatous constituents were not found, though no serial sections were made. The microscopic findings can be summed up by stating that the bulk of the tumor was made up of alveolar carcinomatous formations, with numerous and unbroken transitions to forms which correspond to the chorionepitheliomata, both typical and atypical, of Marchand.

CASE III. The last case, quite recently removed from a youth of twenty-one is also a tumor of the testicle. The subsequent history, if it can be followed, should prove of interest. The tumor has ectodermal, mesodermal and entodermal constituents. Both macroscopically and microscopically it shows papilliferous and cystic forms with hemorrhages. The ectodermal constituents exceed all others. In several spots hornified squamous epithelium is seen, but more often the cells form a single layer lining the cysts, or multiple layers which combine to form complicated adenomatous or papilliform configurations, and not infrequently show a tendency to invade the surrounding stroma. Fusion of cells is common; large syncytial surfaces are not found. About the vessels larger, more deeply staining cells with irregular, dark nuclei of the type of chorionic wandering cells show a tendency to erode the vessel walls.

The most typical picture of chorionepithelioma is presented by my first tumor of the testicle (Case II).

Every quality claimed for the trophoblast is present. The types of cells, their groupings, the relations to the blood vessels, are all in evidence. Whether the other teratomatous elements have escaped my attention because of limited distribution or necrosis, or whether they never attained development is uncertain. That simple tumors may yet be chorionepitheliomatous has been recently asserted by Pick in reference to a carcinoma of the liver, always, however, adding the saving clause that the anlage is teratomatous, the development unequal.

The second testicle tumor (Case III) is surely a teratoma. The ectoderm shows the most active proliferation and also a malignant tendency. Unbroken transitions from simple to stratified epithelium, through papilliferous to solid forms can be traced. The syncytium is not well developed, but cells of the type of chorionic wandering cells abound. Similar tumors, in which, however, the typical syncytium could be more convincingly shown, were described by Pick in the ovary, by Askanazy in the testis. In this atypical variety, by imperceptible transitions, we can get forms resembling carcinoma, alveolar sarcoma, papilloma, or endothelioma, the typical characteristics again cropping out in unexpected places and the varied pictures forming an organic whole.

The metastases of the so-called mediastinal tumor are obvious. Their derivation, on the other hand, will always remain uncertain, for neither the testicles nor the mediastinal tumor were examined. Whether the metastases, of different composition, previously mentioned, are an evidence of other teratomatous constituents from the primary tumor, wherever that may have originated, or represent a second independent growth, must also remain an open question.

In conclusion, without burdening you with a résumé

of the extensive literature, I want to summarize the facts so far collected in this interesting chapter of pathology, and at least suggest such conclusions as seem warranted.

1. An unbroken line of cases leads from the studies of the normal trophoblast through simple hydatid mole, non-malignant and malignant metastasising hydatid and uterine chorionepithelioma to ectopic chorionepithelioma without demonstrable connection with the placental site. The names of Peters, Bonnet, Marchand, Pick, and Schmorl are most closely associated with this work.

2. The studies of Wilms, and particularly of Marchand and Bonnet, have placed the derivation of embryos, teratomata, and dermoids. upon an equal and sure footing. Blastomeres or polecells, liberated from the general complex, resume their growth independent of the general organism, but capable of producing any or all tissues.

3. Among the ectodermal tissues of teratomata, chorionepitheliomatous proliferations have been found in teratomata of the testicle (Schlagenhauser and others), in the ovary (Pick), and in a dermoid of the mediastinum (Ritchie).

4. These chorionepitheliomatous tissues are recognized by their group characteristics, which are those of the normal trophoblast. Their active proliferation causes them to outstrip and overgrow the other tissues, take a leading, though not always sole, part in forming the metastases, and produces a high degree of malignancy in this group of tumors (Pick, Schmorl, and v. Hanse-mann).

5. The chorionepithelium appears in direct continuity with other ectodermal tissues, requiring no special anlage of fetal membranes, and possessing no more

special embryological significance than any other ectodermal constituent of the teratoma (Pick, Risel).

6. Just as the chorionepithelium overgrows the other structures of the teratoma, so the Langhans' cells may outstrip the other types of chorionepithelioid cells and form more simple seeming tumors, which simulate carcinoma, alveolar sarcoma, simple or papilliferous cysts in their structures, but usually betray their origin by large or small areas of typical appearance (Pick, Askansy, my own Case III, etc.)

8. The occurrence of syncytial or plasmodial masses in various degenerations, inflammations, and rapid proliferations, (Bonnet, Aschoff, Babes), robs them of some of their diagnostic value, but does not weaken the doctrine of the specific nature of chorionepithelioma.

8. Chorionepithelium, both in connection with pregnancy and in teratomata, is a strong argument against the parasitic genesis of tumors (Ribbert, Pick).

MORPHOLOGICAL CHARACTERISTICS OF THE BACILLUS ALVEI.

R. J. WILSON, M.D.

Dr. R. J. Wilson gave his reasons for using this organism for demonstrations to students in the University Medical College, as he had done for the last six or seven years. He had found it uniformly useful to the students in making out the characteristics of other organisms later. It was very hard for beginners to see at first the morphological characteristics of the diphtheria bacillus, for instance. After they once saw it, it was always easy

enough to pick it out. The *Bacillus alvei* shows all the morphological characteristics of the diphtheria bacillus and characteristics of various other bacilli. Under certain conditions it shows variations constantly. It is very motile; this motility can be stopped in a moment by specific agglutinating serum which is easy to get. Dr. Wilson showed a chart illustrating various morphological characteristics of the organism. These various forms were shown in microscopical preparations. No. 1 was a vegetative form of anthrax bacillus used as a standard. No. 2 showed the first deviation from the normal, and the one which was most common, that is, the rounded ends. The next most common deviation was vacuolation. The next most common was in the difference in diameter of the body and a difference in staining due usually to granules; this is the type that is characteristic of the diphtheria bacillus. The next deviation from the normal was the presence of metachromatic granules. The granules stained bright red, whereas the body of the bacillus was light blue. The next deviation was the fact that it has an end spore that gives it the appearance of the tetanus bacillus. One spore preparation was stained red by Müller's method and the other blue. No. 9 showed a stain for flagella. No. 10 showed the unusual motility of the organism. No. 11 showed cessation of motion and clumping, the result of agglutinating substances. The only stains used for this organism, except in the case of flagella, were Loeffler's methylene blue and carbol fuchsin. The only media used were ordinary nutrient broth and ordinary nutrient agar, with the exception of one culture which was grown on Loeffler's blood serum. It was then necessary to use only two stains and two media to get all these things. Any beginner could make these stains. Besides being easy to demonstrate

by stains and by its agglutinating substance, the organism was especially good for demonstrating the resistance of bacteria to heat and chemicals. It stood about midway in resistance to heat between the anthrax spore and the typhoid bacillus. The typhoid bacillus is killed by being subjected to a temperature of 70° C. for 15 minutes. This organism is unaffected. When the organism is placed in an Arnold sterilizer it is destroyed, while the anthrax is unaffected. The anthrax is killed in the autoclave. This particular organism was isolated from the tonsils of a patient suspected of having diphtheria. It is frequently seen in cultures coming from throats. It seems to be a species of the *Bacillus alvei* described in *Baumgarten's Jahresbericht* for 1895, and also more completely in the *Centralblatt für Bakteriologie* for 1904.

MYCOTIC THROMBOSIS OF THE RENAL ARTERY.

E. MOSCHCOWITZ, M.D.

Through the kindness of Dr. Hodenpyl, Dr. E. Moschcowitz presented a specimen of mycotic thrombosis of the renal artery. He had been able to obtain but few facts concerning the clinical history, except that the patient had an ulcerative endocarditis with streptococcaemia. At autopsy the kidney was found to be practically destroyed by infarcts, only very little of the normal kidney tissue remaining. The renal artery appeared on cross section as though it had been completely thrombosed. Microscopically it showed the ordinary picture of an anaemic infarct.

MELANO-SARCOMA WITH NUMEROUS METASTASES.

F. C. WOOD, M.D.

On September 30, 1902, the patient applied to the service of Dr. Thomas at St. Luke's Hospital because of a tumor on the back. She had had a flat, brown mole between the shoulders since her birth. Three months before her application to the Dispensary the tumor began to increase in size and became elevated above the surface. It had rapidly grown to its present size. Clothing rubbed the growth and the patient complained of soreness and discharge from the ulceration on the surface. The woman was thirty years of age. She was well nourished; her color was good. On a level with the angle of the scapula and to the right of the median line there was a black pedunculated tumor, about 5 cm. in diameter and 2 cm. in thickness. The surface was rough and moistened with a foul smelling discharge. It was tender and bled easily on manipulation. Below and contiguous with the peduncle of this growth was an area of black pigmentation about 4 by 6 cm. The irregularly circular edge was slightly raised. Scattered about one segment of this black area were a few small spots of normally colored skin. The tumor was excised, the line of excision extending outside to a considerable distance from the black line.

The patient was re-admitted to St. Luke's Hospital with a recurrence in March, 1905, at which time a large area of skin containing blackish nodules was removed from the back.

In September, 1905, she again returned. The wound on the back had not completely healed and she reported that about the middle of April she had noticed several

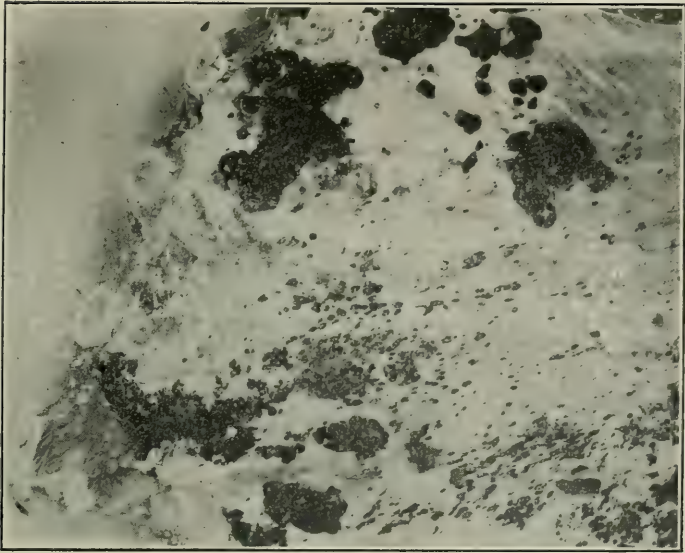


FIG. I. Inner surface of Pleura showing metastatic tumors.

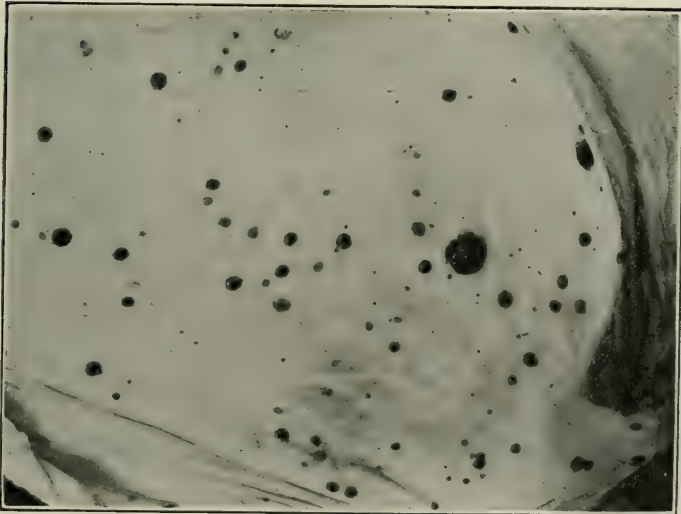


FIG. II. Inner surface of bladder showing metastatic tumors.

small black nodules under the left axilla and over the right breast. These nodules had increased in size until they were the dimensions of a hazel nut. A month ago the left axilla became sore and a lump the size of a lemon had grown there. This was very painful. Two weeks ago the left eye became painful and protruded slightly, and the eyelid drooped. The sight was very much impaired. The whole side of the head ached. The patient was in a poor condition, very weak and anaemic. Examination at this time showed that she was still well nourished. The left eyelid was paralyzed and the sight was blurred. No tumors could be noticed on ophthalmoscopic examination. The skin over some portions of the face showed slight irregular anaesthesias. On the interscapular region there was a stellate shaped scar from the previous operation. The skin surrounding this scar was infiltrated for a distance of 2 to 4 cm. with numerous bluish black nodules varying in size from a pin head to an almond. On the right chest there were three distinct nodules, hard, bluish black in color, and the size of an almond. On the left axilla there was a mass, not adherent, hard, tender, and painful. The nodes in the right axilla were not affected.

The urine contained a trace of albumin but was not noted to turn black on standing.

At autopsy the conditions found were chiefly as follows:—The right breast was excised and showed the nodules which were mentioned in the history. There were three large ones and a series of very small blackish nodules. On cutting up the breast melanotic tumors could be seen scattered all through the fatty tissue. These metastases were interesting because the tumor was primary in the back and the nodules had evidently been transferred forward through the superficial vessels of the

skin or from the pleura. They probably antedated the lung metastases as the woman had noticed them for three months.

The pleura was covered with large, shaggy masses of this new growth, black masses which could be picked off. The lungs were filled with metastatic nodules, some black, others partially white. The pigment formation had not been very complete in the larger nodules. The surface of the lung showed numerous black nodules. Along the anterior border of the right lung there was a fringe of melanotic growth. The heart showed numerous melanotic nodules on section, while the whole surface of the heart was speckled with little pin-head metastases. The bronchial nodes were also large and filled with pigmented growth.

The liver, which weighed ten pounds, was practically filled with nodules. A fresh preparation of the liver showed the coloring of the growth and the enormous number of these mitotic growths, ranging in size from two cm. to a pin-head. The spleen, when opened, showed four nodules, three black ones and one white, one in which the pigment had not formed. The surface of the pancreas was studded with fine metastatic tumors. There was a large tumor on the surface of the organ, and the cut section showed metastatic growths. The kidney contained small tumors, and, curiously enough, the pelvis contained a considerable number. The mucous membrane of the bladder was also covered with small shaggy tumors which could be brushed off the surface. The mesentery and omentum looked like an advanced miliary tuberculosis. On holding the mesentery up one could see along the course of the vessels a large number of tumors, most of them very small, some pigmented and some not. Parts of the omentum which had been re-

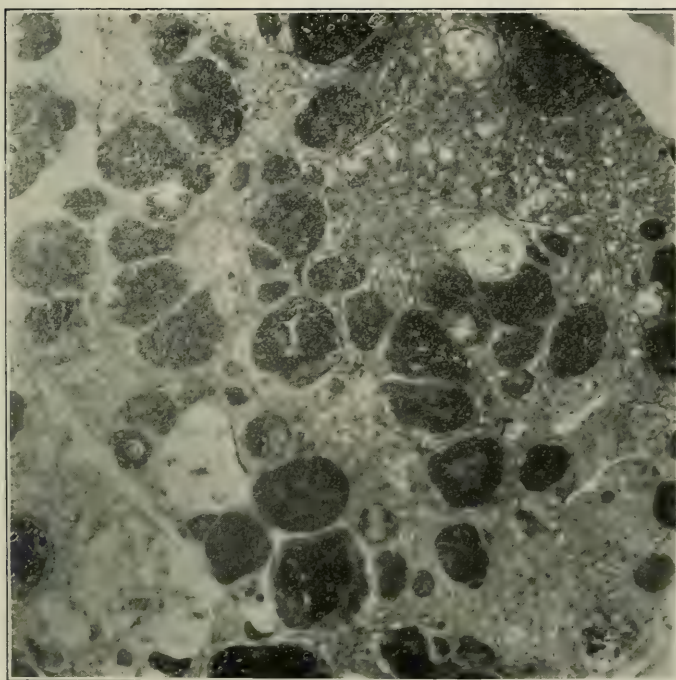


FIG. III. Section of liver showing pigmented and non-pigmented tumors.

moved showed the same speckling with the melanotic tumors. The dura had a few nodules in it. The brain had a few on the upper surface. The pons, the optic nerve, and the upper surface of the cerebellum showed a large number of fine tumors. In the pons on the patient's right side was a large tumor, about 1.5 cm. in diameter. It was curious that there should have been such extensive involvement of the brain with so few symptoms. There were no tumors in the eye and none on the retina. The bone marrow was brown in color, and when squeezed from the rib formed a thick, pasty, brownish fluid. Sections of the liver showed that the growth not only involved the liver but that all of the capillaries contained large numbers of the tumor cells.

The case was interesting from the extreme degree of dissemination of the tumors. As regards diagnosis, there was some question as to whether the tumor should be called melano-sarcoma or melano-epithelioma. The primary growth in the skin was alveolar in arrangement but no one seeing the sections of the metastases would hesitate to call the growth a sarcoma.

A CASE OF RUPTURED AORTIC ANEURISM.

E. P. BERNSTEIN, M.D.

Dr. E. P. Bernstein presented a case of ruptured aortic aneurism, saying that while these cases were rather common the one he had to show had some minor details of interest. The patient, a man fifty years of age, was admitted to the Mount Sinai Hospital in May, 1905. His past history, with the exception of a chancre thirty

years ago, revealed nothing of importance. His present history dated back to a period of four and one-half months, when he began to cough and developed a husky voice, both of which symptoms gradually became more severe. No pain in the chest or on swallowing; no hæmoptysis. Some loss of weight and strength.

The physical examination gave a picture of a disseminated carcinoma of the lung or pleura with metastases in the mediastinal nodes. The left lung posteriorly showed dullness from spine to angle of scapula, with diminished voice, breathing and fremitus; while from the angle of the scapula to the base there was absolute flatness, absent breathing and diminished fremitus. The heart showed no enlargement and no murmurs were to be heard. The pulses were equal, regular, of fair force and tension. Laryngeal examination showed a beginning left recurrent paralysis which was supposed to be due to involvement of the nerve in a mediastinal deposit. The remainder of the physical examination was negative. While an aneurism was thought of the absence of dullness and murmurs excluded this diagnosis.

Six weeks after admission, while talking to his relatives, he suddenly had a severe pulmonary hemorrhage and died in spite of active treatment.

The autopsy, performed about three hours after death, showed that the whole clinical picture was due to an aneurism of the descending portion of the arch of the aorta which had ruptured into the left bronchus. The post-mortem examination showed the following points of interest:—

I. *Larynx*.—The tip of the epiglottis was thickened and atheromatous. Immediately above the left arytenoid cartilage, its lower edge on a level with the false vocal cord, was an ulcer, circular in shape, the size of a

French pea, with a distinct depression in the center—possibly a broken down gummatous tumor. The left true cord was thinner than the right and showed a distinct concavity occupying its posterior half. The posterior crico-arytenoid muscles showed a marked difference in volume, the left being much smaller, paler, and less consistent than the right.

II. *The Left Bronchus*.—About 0.75 cm. from its bifurcation, on its posterior wall, was an opening which easily admitted a large sized probe, communicating with the aortic aneurism. To the right and slightly below this opening were two dark red, bulging portions of bronchial mucous membrane separated from the aneurismal sac by but a thin partition.

III. *Left Lung*.—The left lung was smaller than the right. The entire lower lobe and the lower half of the upper lobe were extremely firm in consistency, but not friable. On section, the parenchyma appeared dry, showing throughout fibrosis, anthracosis, and atelectasis, with numerous bronchiectatic cavities varying in size from a millet seed to a pea.

IV. *Heart*.—The heart showed an interstitial myocarditis with thickening of the mitral and aortic flaps. The coronary arteries were atheromatous.

V. *Aorta*.—The aorta showed throughout its entire extent numerous thick atheromatous plaques, most marked in its thoracic portion. In the arch of the aorta were to be seen several old depressed scars, probably syphilitic in origin. The entire arch was dilated, particularly so in the third or descending portion. Here, from the superior surface extending upward, and lying to the left and behind the left bronchus, was an aneurismal sac about the size of a small hen's egg, its wall covered by a fresh clot; and about one cm. from its apex was a perfo-

ration leading into the left bronchus just below its bifurcation. Exactly opposite the opening of this sac, namely, on the inferior surface of the third portion of the aorta, was a second shallow aneurism extending downwards. The remaining organs showed nothing of interest.

The point of interest in this case was the failure to reach a correct diagnosis. It was strange that such a large aneurism should give no murmur and not be recognized during life. Had the case not come to autopsy it would have been put down as a disseminated carcinoma with metastases in the mediastinum.

A CASE OF EMBOLIC ANEURISMS.

E. LIBMAN, M.D.

Last Spring I had the opportunity of presenting to this Society three cases of embolic aneurisms. The case which I wish to refer to to-night differs in some respects from those previously presented.

The first case of embolic aneurism was described by Tufnell in 1853. In 1873 Ponfick described some cases of embolic aneurism in which he believed that the aneurisms were due to the influence of the embolus on the wall of the artery, particularly if the embolism were a calcareous one. Later a number of other authors showed that these aneurisms usually occurred with acute infective endocarditis, and the opinion has gained ground that these aneurisms are always due to the effect of bacteria-carrying emboli. The case which I wish to present to-night brings up the question whether it is not possible to have an aneurism occur in the way which Ponfick has suggested.

The patient was admitted to my service at Mt. Sinai Hospital on June 26, of this year. He was a man, twenty-two years of age, who had had measles and scarlet fever in childhood, small-pox at the age of two, and pneumonia at two and one-half years. Up to last winter he had not been sick in any way. At that time he had some pain and redness, but no swelling, in the left hip and in both knee joints. There were no cardiac symptoms until about a month ago.

Present Illness: About one month ago the patient began to cough and expectorate bloody mucus. There was cardiac palpitation and a sense of distress over the precordium. During this time he has had severe pain in both knees. The knees were red but not swollen about two months ago.

On admission the patient was found to have an aortic insufficiency. Because of a very marked rough thrill felt in the vessels of the neck it was suspected that there were large vegetations. At this time his temperature ranged between 98° and 102° F. About a week after admission he complained of pain in the left groin; pressure upon the femoral artery caused pain. There was a distinct thrill present in the left femoral and the pulse below had disappeared. There was a systolic murmur in the artery at the point of tenderness.

July 14. There is a petechial spot in the right lower conjunctiva. The case was watched closely as it was suspected that an embolic aneurism had developed. This occurred within ten days. It was located apparently above the point of closure of the femoral. There were present a thrill and systolic murmur; later a double murmur and a distinct enlargement of the artery. The temperature ranged between 99° and 104° F., being very irregular.

On August 6, the patient died suddenly.

During the course of the illness the leucocyte count varied between 6,600 and 9,200. The urine showed no red blood cells at any time; occasionally there was a trace of albumin with a few leucocytes and an occasional hyaline cast.

Three blood cultures were made, 15 c.c. being used twice and 11 c.c. once. The last blood culture was taken a few days before death. The blood was inoculated on bouillons and agars with and without the addition of glucose or serum or both. The Wasserman medium was also used. Part of the material was cultivated anaerobically. All three blood cultures were negative.

The autopsy was performed under great difficulties. Fortunately we were able to obtain the heart and kidneys in good condition, but the iliac artery had to be removed through an incision in the lateral scrotal fold. The specimen is for that reason not in good condition for study; nevertheless, it shows sufficiently well the important points. Without going into too much detail the following were the conditions found.

At the lower part of the iliac artery there is a sacculated aneurism about 2 cm. in diameter. There is some calcareous material present in the vessel. The intima at the entrance to the aneurism is not cut off, but goes directly into the sac.

The lungs show brown induration.

The mitral valve and the chordae tendinae showed some old verrucose vegetations. The aortic valves were thickened, shrunk, and insufficient. On two of the flaps there were some small old vegetations. The anterior flap was ulcerated and hanging from it was a friable, calcareous mass. The aortic flap of the mitral valve showed an aneurism the size of a large cherry projecting

into the left auricle and obstructing the auriculo-ventricular orifice.

The spleen showed one small infarction.

The kidneys showed some chronic nephritis. In the right kidney there was a small aneurism of one of the smaller branches of the renal artery. The vessel entering it contained a recent thrombus. The kidney cortex about the aneurism presented a large, anemic, infarcted area.

The cultures from the heart are unreliable as the organ had to be dragged down through the abdominal cavity; likewise the aneurism of the femoral artery was contaminated because of the method of removal. The cultures from the surface of the spleen, however, taken on a large number of media proved to be absolutely sterile.

Considering that the blood cultures during life were all sterile and the spleen culture postmortem was negative, and that the aneurism of the iliac artery was of a different type from that which has been found in cases of infective embolism, I believe that it is possible that in this case the aneurism of the iliac artery may have been non-mycotic in character.

It is not difficult to find bacteria in the blood in cases of bacterial endocarditis. I appreciate, of course, that in some of the cases due to attenuated diplococci or streptococci, the organisms are difficult to find, but, as a rule, in three cultures, one succeeds in finding them.

MULTIPLE CYSTS OF THE MESENTERY.

D. S. D. JESSUP, M.D.

Dr. D. S. D. Jessup presented a specimen from a case of multiple cysts of the mesentery, for which he was indebted to Dr. Proctor of the Englewood Hospital. The patient was a boy of twelve years, who entered the hospital about a year ago with a history of swelling of the abdomen for several months. The boy was not very well nourished. He remained in the hospital for ten days. He returned in March with increased swelling of the abdomen. The abdomen was aspirated and examination showed a fluid of a dark greenish brown color, specific gravity, 1.022; albumin present; no bile; no sugar. Microscopical examination showed cholesterin crystals and some fat globules. Examination of a second specimen showed fluid of a specific gravity of 1.020; albumin, 3 per cent.; no bile; no sugar; cholesterin crystals and fat globules. There was 0.05 per cent. of fat. A number of white cells were found, about 80 per cent. of which were eosinophiles. The boy was quite anaemic. He was kept under observation for six weeks, when an exploratory laparotomy was done. On opening the abdomen multiple cysts were found in the mesentery and were removed in two large masses. The operation lasted for two or three hours, and the cysts were so tangled up with the gut that Dr. Proctor was compelled to remove about ten inches of the small intestine with the cysts. A number of these cysts have been punctured and the contents evacuated, so that the whole mass is somewhat smaller than when first exposed. The boy made an uneventful recovery. Examination of these cysts showed in most cases a fluid similar to the fluid described, some was lighter in color and contained chyle. A number of

small nodules were scattered through the walls of the cysts. They were made up of brown granular material, almost entirely cholesterin crystals. Sections of the cyst wall showed no lining epithelium. In regard to the origin of the cysts it was difficult to decide absolutely. Cysts have been classified as echinococcus cysts, congenital cysts, including dermoid cysts, and malignant cysts. It seemed to Dr. Jessup that such a cyst as the one shown would probably come under the class of congenital cysts. The case was interesting from the standpoint of diagnosis, and because of the favorable outcome after the removal of so extensive a growth.

A CASE OF SPIROCHÆTAL INFECTION IN MAN.

CHARLES NORRIS, M.D.

For my assistants, Drs. Pappenheimer and Flournoy, I desire to report briefly at the present time a case of spirochætal infection. The patient entered the service of Dr. Robert J. Carlisle at Bellevue Hospital. I shall not enter, except in a very brief way, upon the clinical history of the case, which will be reported more fully by Dr. Carlisle.

The patient had been all his life making sea voyages to various parts of the world. His previous history had been uneventful, with the exception of a single attack of sickness when in Calcutta in 1893. He is not certain whether his blood was then examined. In July of this year he shipped as an assistant steward on the SS. "Denver" of the Mallory line, and stayed for five days in

Galveston, sleeping on board, and returned on the same steamer to New York, arriving on August 10. Two days later he was taken with a chill, accompanied with fever, prostration and pains in the bones. He was admitted to the hospital August 15, with a temperature of 102.4° which reached normal the following morning. The evening of the second day the temperature rose to 101.6° , falling abruptly to subnormal within 24 hours. For four days it remained normal, then rose within 24 hours to 105.4° ; then again it fell abruptly to subnormal by the evening. Ten days of subnormal temperature followed, with the exception of two slight elevations to about 100° . On August 31, the temperature again rose to 103° , falling within 24 hours to normal. At this time, examination of the blood for malaria parasites, by Dr. Heitlinger, House Physician of the Third Medical Division, showed the presence of a few spirochætae. With the fall of temperature, the organisms disappeared from the blood. They were again found on September 10, (ten days later), the temperature rising the previous night, reaching 103.4° in the evening. The next day the temperature fell abruptly and has remained normal up to the present time.

The following is a brief summary of the animal inoculations that have been made.

On September 10, a small Rhesus monkey was inoculated with 3 c.c. of blood, the patient having at that time fever and organisms in the circulating blood. Small numbers of spirochetes appeared in the blood of this monkey, 48 hours after inoculation. The monkey at this time showed a slight rise of temperature, but had no visible signs of illness. The organisms persisted for three days, then an interval of apyrexia lasting five days followed, during which time the blood was free from organisms. Since that time the monkey has suffered two

relapses, in the second relapse towards the end of the paroxysm the organisms being found in large numbers, on the average three or four or more to the field, and frequently present as tangled masses.

A small Java monkey was inoculated with the blood of Rhesus I, during the latter's first paroxysm. An incubation period of three days followed. The Java then showed febrile periods similar in duration and character to those described for Rhesus I. The Java up to the present time has had two relapses each accompanied by spirochetes in the circulating blood. The third monkey, a large Rhesus II, was inoculated with the blood of the Java, and likewise developed a spirochætal infection of a mild type, up to the present time having had but one relapse. A third Rhesus, a female, was inoculated with the filtrate of several c.c. of blood from the Java monkey, showing numerous spirochetes. After two weeks no infection has occurred.

We have obtained evidence that the spirochetes multiply considerably in the blood of young rabbits inoculated intravenously, but that they disappear after one to two days. Guinea pigs, intraperitoneally, and a goose, subcutaneously, have been inoculated, but without infection.

Numerous unsuccessful attempts have been made to obtain cultures. A description of the morphology is omitted, as the specimens under the microscope show this much better than any description that I can give. The organisms in the blood of the patient and the monkeys are similar in appearance, and resemble in all respects the description and photographs of Obermeier's spirillum. They vary considerably in length and in the number of turns. Every transition exists in the closeness of these turns. Many of the longer forms show an attenuation

or unstained portion in the center, suggesting fragmentation or fission. In the fresh preparations the organisms exhibit three distinct forms of motility, similar to those that have been described for the *Spirillum* of Obermeier, and of the spirillum fever of geese. The organisms stain with all the ordinary aniline dyes and decolorize by Gram's stain. For the routine examination of the blood we have used Wright's stain, the organisms taking a deep blue tint.

The case reported is of interest from many points of view. So far as I have been able to ascertain it is the first case which has been reported in this country of spirochaetal infection verified by microscopic examination of the blood. Another case, I understand, has recently been observed in one of the hospitals of this city.

Relapsing fever epidemics have in former years been recorded, all of them prior, however, to the announcement by Obermeier, in 1873, of the constant presence of spirochetes in the blood of persons suffering from relapsing fever. An interesting and complete account of the last epidemic is found in the report of the Board of Health of New York for 1870, as reported by the sanitary committee on relapsing fever by Stephen Smith. This epidemic was the first recognized appearance of relapsing fever in New York. It spread chiefly by the contact of the sick with the well and it was directly amenable to the most simple measures of prevention. Its victims belonged for the most part to the class of destitute persons, vagrant or homeless wanderers. To quote from the report, the recorded history of relapsing fever in the United States previous to 1869, is very brief. It seems to have been first recognized in 1844 by Prof. Meredith Clymer in Philadelphia. The disease was then prevalent in Ireland,

and was introduced by Irish emigrants from Liverpool. The cases observed had no second relapse.

Cases of relapsing fever were reported by Dr. Dubois in New York in 1847-48, and by Prof. Flint in Buffalo in 1850-51. These cases were in recently arrived emigrants from localities where the disease was prevalent. The first cases of relapsing fever in New York of the epidemic of 1869-70, which were definitely and satisfactorily traced out, occurred on October 6, 1869, in a building occupied by three families which received vagrant lodgers and beggars. Thirteen persons were found to have had fever in the house and numerous sick lodgers had strayed to other lodgings, and in two or more such houses the fever had appeared. The total number received at Bellevue Hospital was 238, twelve of which occurred in the hospital. Two physicians, several nurses, and patients who were in immediate contact with the sick were attacked. There were so many cases that a relapsing fever hospital was opened on Hart's Island on February 28, 1870, which remained open till August 8, of the same year. The total number of cases admitted was 1673, with fifteen deaths.

In 1869-70, cases were observed in various towns in New Jersey, which were imported from New York, and also in Philadelphia. Dr. Parry, who observed the epidemic in the city, reports several cases in which the infection seems to have been clearly traced to fomites, an observation of great importance.

The last case recognized as relapsing fever occurred in New York in 1873.

It is believed that the fever which Hippocrates described as prevailing two thousand years ago in the Island of Thasus, off the coast of Thrace, resembled relapsing fever very closely in most of its characters, including an intermission of five or seven days between the febrile at-

tacks. The first authentic description of the fever is attributed to Dr. Rutley in the chronological history of the diseases of Dublin in 1739. A big epidemic occurred in Ireland in 1847-48, then none up to 1862. In Peru, there was an epidemic in 1854, and in 1859 in Bolivia and Chili. According to Murchison, relapsing fever does not seem to have been observed on the continent prior to 1847.

The epidemic of relapsing fever which broke out in August, 1864, in St. Petersburg, created great alarm, as the nature of relapsing fever was not at first recognized. In that city, from August, 1864, to March, 1865, there were present in the hospitals 7,097 cases of typhus, and 7,625 of relapsing fever. Dr. Maréché has given an account of the very extensive prevalence of the fever in Pekin and throughout Northern China, in 1864, and Carter has reported epidemics of this disease in India.

A big epidemic prevailed in London, in 1869. According to Murchison, the disease spread so rapidly that the resources of the city were taxed to the utmost to find accommodations for persons attacked with it. He believed that the tramping vagrants had largely assisted in the distribution of the complaint over London.

It was not until the epidemic of 1843, that relapsing fever was distinguished from typhus, principally through the studies of Prof. Henderson and, later, those of Jenner.

The research work of the past few years under the auspices of the English, French and German Governments upon the tropical diseases of man and animals, has brought to light, especially in South Africa, the discovery of the etiological agents of various hitherto little understood diseases.

Since the discovery of the *Spirochæta anserina* by

Sacharoff in 1890, which causes the spirillum fever or septicaemia of geese and other birds, to which infection monkeys are immune, other spirillary infections have been noted in both animals and man. A. Theiler has described what he calls "La Spirillose du bétail", caused by a spirochete which is found in the blood where it produces an anaemia. It is seen principally among the cattle which are in bad condition. Like the piroplasma begemini it lives in the blood of immune cattle, as the disease has been inoculated with the blood of such cattle. The disease is conveyed through the agency of the blue tick, which is the intermediate host. Like the piroplasma, the infective agent passes into the egg, and is inoculated by the larvae. Theiler believes that the spirochete is a parasitic protozoon. He has also noted the association of spirochetes and trypanosomes in common red water fever and in Rhodesian red water fever. The fowl disease of Brazil is also due to a spirochete. The fowl disease is transmitted like the Texas and Rhodesian fevers, and those of horses, sheep and dogs, which are due to as many species of piroplasma, by the agency of ticks, the ticks concerned being different in different countries.

In July of this year, Ronald Ross read a paper by Dr. John H. Todd and the late Everett Dutton (who died of the spirillum fever in his third or fourth relapse) before the section on tropical diseases of the British Medical Association, upon the nature of human tick fever in the eastern part of the Congo Free State. The conclusions drawn by these observers were:—1. That tick fever is clinically identical with relapsing fever, and has for a pathogenic agent a spirillum. 2. That the spirillum is probably *Spirillum Obermeier*. 3. That the tick *Ornithodoros moubata* can transmit the spirillum from

animal to animal. 4. That the transmission is probably not merely mechanical but that some developmental process is carried on in the tick. Ross and Milne have also described the tick fever of Uganda in Africa. In twelve cases of spirillum fever they found that it might be exceedingly rare in the blood taken even at the highest of the fever, from cases with well marked clinical symptoms, occasionally only three examples being found in a large film of blood. All the cases made a good recovery. Natives attributed the disease to the bite of a tick in their huts of their native camps.

In the light of Marchoux and Salimbeni's work upon the transmission of spirillum disease of fowls by ticks, Ross considers it probable that the disease in man also is inoculated by the bite of infected ticks, and that there may be other parasites conveyed to man by ticks, and so it is possible that more than one form of tick fever exists. Spirochetes in the blood of two cases have been observed by J. Cropper in Palestine. One of these was a boy suffering from a quartan type of fever, with numerous malarial parasites, lasting for twenty days. Two spirals were found in the stained specimen and one in the fresh. Hill, in China, has also observed the presence of spirals in the blood slides of cases, but he states that it is rare, as he only found them twice in hundreds of specimens of blood examined.

A number of other accidental findings need not be here recited. It is unnecessary at this time to enter into the interesting question as to the nature of the spirochetes.

Schaudinn considers that the halteridium, one of the haemosporidia in the owl, is the sexual stage of a trypanosome which undergoes a complex form of multiplication both in the *Culex pipiens* and in the blood of the

owl, and then gives rise to the sexual forms of the halteridium. The results obtained by Schaudinn with the leucocytozoon of Danilewsky *Haemamoeba Ziemanni*, were much the same as those for the halteridium.

Schaudinn calls special attention to the agglutination of the small, rapidly dividing forms of the trypanosome. The resulting clumps are made up of indifferent cells which come together by their posterior ends, and hence the flagella are on the outside of the rosette, whereas in the trypanosome the whips are directed centrally. It is because of this type that Schaudinn designates this form as a spirochete. He further regards the spirillum of recurrent fever and of geese as essentially the same as the spirochete, or *Haemamoeba Ziemanni*. Schaudinn believes that there can be little doubt that these will be shown to be trypanosomes and hence unrelated to the bacteria. Novy and McNeal have shown that Schaudinn's interpretation of what he has seen is subject to grave doubt and they state that his two types of trypanosome and spirochete are really two forms of one species.

However this may be, the spirochætal forms of the trypanosome as depicted by Novy and McNeal have not the slightest resemblance either to our spirillum or to the Obermeier and anserina, as shown by the photographs.

There is no time to enter into a review of this interesting group of organisms which is now occupying the attention of the world, especially in reference to syphilis. Since the recognition of the *Spirillum denticola* by Miller, they have been found in many lesions of the mouth and gum, in the intestinal contents, in diarrhœal stools, and by myself in a case of liver abscess in association with anaerobic bacteria, in various skin lesions, and in lesions of the internal organs which have been lately reported. Further, Castellani has shown the presence of

spirochetes in two cases of Yaws at Colombo, Ceylon, an important observation, since by some this disease is supposed to be syphilis, but by others, another and distinct non-hereditary, but markedly contagious, disease.

The question may be briefly discussed. Is our case one of relapsing fever due to the *Spirillum Obermeieri*? The question can be approached from several points.

First, clinically, our case differs considerably from the reported cases of relapsing fever observed during epidemics, in the mildness of the symptoms, short duration of the fever, the length of time between the relapses, and in the scarcity of the organisms found in the circulating blood. This distinction alone, I admit, is no argument for or against the identity of our organism with the *Spirillum Obermeieri*.

If it be assumed that the case is one of relapsing fever, the history of the patient as to previous illness being correct, we must suppose either that he had relapsing fever in Calcutta in 1893, or that it was acquired in Galveston, the time spent there and the five days of the voyage representing the incubation period usually given for relapsing fever. If the former supposition be correct, he has harbored the organisms in his system for twelve years without untoward effects until his recent illness. No facts in our possession up to date justify this assumption. If the latter supposition is correct, namely, that he has acquired relapsing fever in Galveston, is it not singular that no other cases of this fever, which is supposed to be markedly infectious, have been reported from Galveston, Porto Rico, and the various Mediterranean ports which the patient visited during the last year? However, no matter how we agree, a second infection cannot be excluded, since relapsing fever does not confer any lasting immunity.

Secondly, animal reaction. This gives little aid as monkeys are readily inoculated with the *Spirillum Obermeieri* as in our case. The disease we transmitted to our monkeys is much milder than the experimental spirillum infection of those animals reported by various observers. Relapses in the latter have rarely been noted; by one observer in one out of eight monkeys. Other observers have never seen relapses. In our case the three monkeys have all had relapses; the first Rhesus has already had three, and further observations may show more.

Thirdly, morphology alone gives no infallible guide in the differentiation of organisms of this group. Thus the *Spirochæta anserina* resembles the *Obermeieri* in apparently every respect, and yet the animal reactions are wholly different.

In conclusion it may be said, first, that our case clinically resembles in its mildness and in some other features, so-called tick fever of certain parts of Africa. The identity of the spirochetes found in this disease cannot be said to be satisfactorily established.

Secondly, we wish to call attention to the probability of mild spirochætal infection more or less constantly occurring in sailors or travelers coming from southern climates into the port of New York.

Thirdly, the probability that the fever is not the relapsing fever which has occurred in epidemics and which has been regularly imported from the Continent into the States.

Fourthly, the possibility of infection being communicated from person to person through the bites of ticks, bed-bugs, and through wounds.

Discussion.

DR. JAMES EWING said that he had had the opportunity of looking at a number of specimens of blood from the patient and from some of the monkeys. One point of interest was the variation in the morphology of these parasites. Some were extremely long, very much longer than the extant photographs of the *Spirillum* of Obermeier. On the other hand others were much shorter, approaching many of the ordinary spirochætae found in the mucous membranes of the mouth. These variations made the morphology a very poor guide in the identification of the organism.

DR. E. LIBMAN said he would like to refer to an interesting case which he had seen during the summer in Chicago, being induced to do so by the attention which Dr. Norris had drawn to the importation of diseases hitherto occurring in tropical countries only. The case was in all probability the first case of "dum-dum fever" or kala-azar seen in this country, although the spleen was not aspirated in order to determine the presence of the Donovan-Leishmann bodies. The patient was a boy twelve years of age, with a very large spleen and marked anemia. The leucocyte count was 1,200. Fever was present, irregular in character. The patient has recently come from Calcutta. Dr. Libman said that when he suggested that before any diagnosis could be made it would be necessary to aspirate the spleen to look for the parasite, the father volunteered the information that the boy's brother had died near Calcutta a year before with a diagnosis of "dum-dum fever". He stated further that he had presented the same symptoms as the child who was at present sick, and that the latter had already developed the symptoms before leaving India.

OBSERVATIONS ON SPIROCHÆTAE IN
SYPHILIS.

JAMES EWING, M.D.

During the past summer I examined material from thirty-six cases of syphilis in search of the *Spirochæta pallida* of Schaudinn and Hoffman. My chief object was to ascertain what clinical value a reasonably prolonged search for the spirochæta might have in the diagnosis of syphilis. For access to the cases I am greatly indebted to Dr. Edgerton, of the Cornell Dispensary, to Dr. Osgood, of the Bellevue Dispensary, to Dr. Charles Norris, and to Dr. H. A. Janeway. For the demonstration of the spirochæta the stains employed were Giemsa's, the Nocht-Romanowsky, and a strong watery solution of Kresylecht-violet, as recommended by Davidsohn (*Berl. klin. Woch.*, 1905, p. 985). The best results were obtained by freshly prepared Nocht-Romanosky stain. Giemsa's stain gave excellent results, as did also the simple solution of Kresylecht-violet. I have not used any of the more rapid stains such as carbolic gentian-violet, but carbolic fuchsin and some other methods gave unsatisfactory results. Specimens were fixed ten minutes in methyl alcohol and stained twenty to twenty-four hours.

Of the thirty-six cases, *Spirochæta pallida* was demonstrated in twenty, often in several lesions of the same case.

Chancres. Eleven chancres, nine of the prepuce, one of the lip, and one of the finger, were examined, with positive results in five. In all of these the serum squeezed from the cleansed lesion was used. The spirochætae were never numerous, and in one case, two hours were spent before a single typical *Sp. pallida* was encountered, and six remained negative after one hour's search.

Cutaneous lesions, secondary or tertiary, were examined in eighteen cases with eleven positive results. Maculo-papular eruptions gave three positive and three negative results; postular eruption, one negative; tubercular eruption, three positive and two negative; moist erosions, four positive and one negative; and one tertiary rupial or tubercular lesion gave a negative result.

The cutaneous lesions contained more numerous spirochætae than any others examined. In one case presenting three small tubercular lesions on the neck and moderate adenopathy, duration six months, the organisms were extremely abundant, as many as twenty appearing in one field of the immersion lens. In another similar case, raised, cyanotic, rather soft, slightly scabbing or glazed lesions on the back of the neck yielded many clumps containing from ten to seventy-five and more of typical *Sp. pallidac*. The largest proportion of successful results was obtained from moist erosions about the genitals, but the ordinary maculo-papular eruption seems to contain spirochætae readily demonstrable in most cases.

Mucous patches of the mouth were examined in six of the early cases. The whitened epithelium of the patch was raised by a scalpel or forceps and the exuded serum carefully removed by a platinum loop. It soon became apparent that these lesions always contain spirochætae in considerable numbers. They were sometimes very numerous, once clumps of ten to forty being found. There appeared to be definite chromatin granules in the central portions of some of the clumps. In one ulcer of the trachea *Sp. pallida* was abundant; but in one ulcer of the tonsil only numerous *Sp. refringens* were found, although some of the forms approached the characters of *Sp. pallida*.

Lymph nodes were examined in six cases with negative results in all but one. In the successful case two spirochætæ were found in one hour, one of which was a typical *Sp. pallida*, the other showed looser coils. In one case with abundant typical macular eruption, duration two weeks, general lymphadenitis and mucous patches in the mouth, two enlarged cervical nodes were aspirated three times, but no trace of spirochætæ was found after four hours search. The material contained many clumps of degenerating lymphocytes. In one case with an ulcer of the larynx which yielded *Sp. pallida*, no spirochætæ could be found in spreads of an excised cervical node. In four cases of florid syphilis one or more inguinal nodes were aspirated but no spirochætæ were found among the numerous degenerating lymphocytes, except in one case. In one of these, degenerating bacilli resembling the *B. involutus* of Waelsch (*Cent. f. Bakt.*, 1905, p. 645) were frequently seen. In another case the material contained large numbers of bodies resembling Siegel's *Cytorrhycles luis*. In two cases it was hoped to hasten treatment by the discovery of the spirochætæ before the appearance of the eruption. In one of these the attempt was successful. In all of the examinations of lymph nodes two to four hours or more were spent in the search.

Tertiary lesions.—Four cases were examined. In one an abundant relapsing rupial or large tubercular syphilide failed to give spirochætæ. A large gummatous ulcer of the trachea gave numerous examples apparently of both types. A gummatous ulcer of the tonsil gave numerous *Sp. refringens* and many forms approaching *pallida*, but none typical. In this case numerous bodies resembling *Cytorrhycles luis* of Siegel (*Munch med. Woch.*, 1905, p. 1321) were found. An excised gumma of the brain was negative.

Circulating blood. About two hours were spent on each of three cases in a search for spirochætae in spreads of the blood, with negative results. Noeggerath and Staehelin (*Münch. med. Woch.*, 1905, p. 1481) report the discovery of moderate numbers of spirochætae in the centrifugalized sediment obtained by dissolving 1 c.c. of blood in 10 c.c. of 0.3 per cent. acetic acid. This method was followed in one case of florid syphilis, with abundant macular eruption part of which was just appearing. The result was negative. The possibilities of contamination of such specimens unless drawn from a vein after incision of the skin must be considerable. I squeezed the blood from a puncture of the ear and encountered four varieties of bacteria during the search.

Mercurial treatment seems to affect the numbers of spirochætae very slowly. Most of my cases had received more or less mercury. Six cases in which spirochætae were found had been energetically treated by subcutaneous injections. In one case active treatment for one month failed to reduce the numbers of spirochætae demonstrable in the papules. Many other observers have reported similar results.

Morphology.—*Spirochæta pallida* is a very fine spiral body, 5 to 12 micra in length, with five to ten coils sharply and regularly wound like a corkscrew. It stains with difficulty, requiring three to four hours by Giemsa's or Nocht's stains, or two to three by kresylecht-violet, and is better stained after twenty-four hours in any of these stains. It usually takes a reddish tinge after Giemsa or Nocht, violet after the kresylecht-violet. It has been claimed that *Sp. pallida* may be distinguished from *Sp. refringens* by the fact that the former stains reddish by Giemsa's stain, while the thin forms of the latter take a bluish tinge. I can not agree with this view,

finding that the color taken by both spirochætae depends on the quality and thickness of the surrounding medium, and that either variety may take a reddish or a bluish tinge. In one case the numerous spirochætae found in the serum squeezed from a chancre were typical *Sp. pallida*, except that many of them were nearly straight rods and showed unusually flat coils without the usual sharpness and regularity.

Spirochæta refringens, a common saprophyte of mucous membranes, especially in the mouth, is much thicker, often larger, with three to five loosely and irregularly wound coils. It stains more rapidly by all dyes. Both types of spirochætae show considerable variations in morphology. While the typical *Sp. pallida* is very characteristic and easily distinguished from the typical *Sp. refringens*, some of the spirals found in syphilitic lesions, chancres, papules, etc., are identical in appearance and staining qualities with those found in non-syphilitic lesions. From this point of view one may say that there are transitional forms between *pallida* and *refringens*, without denying that the two species are distinct. When, however, considerable numbers of typical individuals of both types are found associated one may be justified in claiming that the two species exist together. Such association of typical *Sp. pallida* and *Sp. refringens* was observed in six cases; viz., one ulcer of tonsil, one ulcer of trachea, one deep ulcer of prepuce, one tubercular lesion of the skin, and three mucous patches of the mouth. In the great majority of syphilitic lesions of the skin only *Sp. pallida* was found, sometimes in very large numbers. Nevertheless it is an interesting fact that *Sp. refringens* may also be found, probably as a saprophyte, in some of these cutaneous lesions far removed from the usual location of such organisms. In one secondary papular lesion

of the arm associated with a very few *Sp. pallidæ* were many larger forms which must be classified as *Sp. refringens*.

Various non-syphilitic lesions of the genitals were examined and spiral organisms were frequently, but not always, found, sometimes in enormous numbers. The forms of the organisms varied greatly. In several cases of balanitis, large numbers of nearly straight, actively motile threads were encountered together with a few bodies showing the spiral coils of spirochætae. In other cases of balanitis, scrotal eczema and acuminate warts, the great majority of spirochætae exhibited several loose coils as described for *Sp. refringens*. In one case of scrotal eczema with acuminate warts, duration eighteen months, the majority of organisms approached, and many were identical with, the type of *Sp. pallida*. Nevertheless in no non-syphilitic case were the great majority of the organisms of the type of the smallest *Sp. pallida* as is often the case with pure syphilitic cutaneous lesions. The diagnosis of syphilis would seem to require that the great majority of spirals should present the typical characters of *Sp. pallida*. In the non-syphilitic lesions the spirals were usually much more actively motile than were those from syphilitic cases.

In a case of very extensive ulcerating epithelioma of the penis and groin, the surface exudate contained enormous numbers of spirochætae. Most of these would be classed as *Sp. refringens* from their thickness, great length, loose turns, and dense stain. Many others, however, were thinner and more faintly stained than any typical *Sp. pallida* I have seen, while their coils were numerous and very sharp. I do not believe it possible to distinguish many of these forms from the genuine *Sp. pallida*, while not attempting to deny that they were bio-

logically different from the organism of syphilis. An extensive extirpation of the penis, scrotum and groin was performed in this case. The large tumor mass was placed in 5 per cent. formalin which penetrated the tissue slowly, giving time for the post-mortem multiplication of micro-organisms already invading the tissue. Two days later the mass was incised and spreads made from the tissue not yet reached by the formalin. A good many bacteria were found in these spreads, a fact which indicates that the dissemination of spirochætæ was largely cadaveric, although many of them must have been deep enough within the tissues before the operation to have been protected from the formalin. However, very numerous spirochætæ were found in the center of this tumor mass, three inches below the surface. Although the coarse spirochætæ were very abundant on the surface of this tumor, those found in the deeper portions were nearly all of the pale fine texture with sharp coils and indistinguishable from many of the organisms seen in syphilitic lesions.

On the surface of an epithelioma of the cheek large numbers of large, actively motile spirals and some fine, less motile ones, were demonstrated. Some of these were obtained from the connective tissue beneath the ulcer, but none could be found after an hour's search in spreads from two submaxillary lymph nodes invaded by the tumor. A few of the spirals from the ulcerating surface were indistinguishable from *Sp. pallida*, but the majority were of the type of *Sp. refringens*. If saprophytic spirochætæ are capable of living, not only on, but to a slight extent in inflamed tissues, it would seem possible that they might be carried through a series of experimental lesions in monkeys. It may be noted that several

varieties of bacteria are known to appear in this way in a series of vaccine lesions.

The present series of cases contains a comparatively small proportion of successful results. This is partly owing to the limited time devoted to the examination of some cases, not more than one hour having been spent on the external lesions, and two to four or more on the lymph nodes. I have drawn the impression, however, that if one must limit the diagnosis of syphilis to lesions in which perfectly typical *Sp. pallidæ* are demonstrable by ordinary methods, then the present clinical scope of syphilis will be somewhat contracted. This statement applies chiefly to some cutaneous lesions now commonly regarded as syphilitic and to some lesions of the genitals. If one will carefully select his cases and spend several hours in the search, it seems probable that the *Sp. pallida* may be found in every instance. The present series of cases were taken as they applied at the dispensaries and this fact doubtless contributes to the low percentage of successful results.

The nearly constant demonstration of *Sp. pallida* reported in syphilitic lesions, the apparent absence of perfectly typical forms in considerable numbers in other lesions, their frequent presence in the lymph nodes and possibly in the blood, the large numbers reported in some cases of congenital syphilis, and their demonstration in experimental syphilis in the monkey, constitute a formidable array of evidence in favor of the view that *Sp. pallida* is the cause of syphilis. Nevertheless, a number of uncertainties seem to surround the interpretation of many of the results of observation.

While the majority of reported examinations of lymph nodes were successful, not a few failures are being recorded. In some cases only one or two spirochætae

were found after one or two hours search and mention has seldom been made of the presence of other micro-organisms noted during such prolonged search. In some of my cases, during a negative search for spirochætæ, various bacteria were observed in the spreads from lymph nodes. As saprophytic spirochætæ seem capable of penetrating tissues, their occurrence in lymph nodes would be more convincing evidence if nodes more distant from the point of entry were examined. The discovery of one or two spirals after six or eight hours search in lymph nodes in active syphilis would seem to be somewhat unsatisfactory evidence for the etiological relation of the organism to the disease. We do not yet know how far spirochætæ can penetrate inflamed tissues as a saprophyte or secondary invader. The possibility of mistaking spiral threads of nuclear material for spirochætæ, especially in lymph nodes, must be considered, as such threads may undoubtedly reproduce exactly the forms of all but the most perfect specimens of *Sp. pallida*.

The extreme variation in the number of spirochætæ in syphilitic lesions is a peculiar and puzzling fact. I have found them extremely abundant in some old cutaneous lesions and often extremely scanty in chancres. Likewise they have been reported in enormous numbers in the skin and organs of some cases of congenital syphilis, and absent in others.

The most striking evidence in the present study favoring the view that *Sp. pallida* is the cause of syphilis does not consist in statistics but in the very large numbers of organisms found in the serum from some cutaneous lesions. In these cases the spirochætæ were almost entirely unmixed with other micro-organisms, and in the cases of old tubercular syphilide of the neck in which ten to seventy-five spirals appeared in single fields of the im-

mersion lens, I find it difficult to imagine any other satisfactory explanation than that these organisms were the cause of the lesions. Moreover, the moist erosions about the genitals which are known clinically as very infectious usually contained large numbers of organisms.

Assuming the spirochætae to be the cause of syphilis the indications are that the search for this organism will prove a valuable adjunct in the diagnosis of the disease, but much more extensive observations on non-syphilitic lesions are required before the clinical value of the discovery of the spirochætae can be established.

While I am strongly inclined to regard the spirochætae as the cause of syphilis I consider that the data are at present inadequate to demonstrate the positive claims made for it, not by its discoverers, but by other somewhat less critical observers.

At present the chief difficulties seem to lie in the demonstration that a specific species exists in syphilis, which may not be possible on morphological grounds alone, and in the determination of the power of saprophytic spirochætae to penetrate tissues.

OBSERVATIONS ON SPIROCHÆTAE IN SYPHILIS.

T. W. HASTINGS, M.D.

Dr. T. W. Hastings reported on twenty-eight cases studied for the presence of *Spirochæta pallida*. Among these 28 cases were 10 not syphilis, the cases having been taken at random. The remaining 18 cases were undoubted syphilis. In 9 *Spirochætae pallidae* were demonstrated.

Among the 10 cases not syphilis there were 5 cases of chancroids and one of herpes of the penis, one chronic ulcer of the leg, one eruption on the forearm, thought at the time to be syphilitic, one case of amoebic dysentery with spirilla and *Spirochæta refringens* in the mucous exudate, one case of vaginitis.

The examinations in the 18 cases of undoubted syphilis were distributed as follows: --Serum and blood from eight chancres before the appearance of the secondary lesions, from two after the appearance of secondary lesions; serum from five secondary lesions; serum from three tertiary lesions; serum from the eruption of a congenital case; serum from the oedematous prepuce (phimosis) covering a chancre; serum aspirated from the inguinal glands in five cases.

The specimens were prepared by squeezing the chancres or cutting through the edge and smearing the serum or blood on slides. The material from the papules was obtained by scraping the surface with a Hagedorn needle. From the glands and the deeper portions of the tertiary lesions serum was obtained by aspiration with a "Sub Q" syringe. The smears were fixed in ethylic alcohol for from 20 to 30 minutes, or in methylic alcohol for 10 minutes, and stained with Giemsa's or Nocht's azur stains, or Davidsohn's kresylviolet for from 12 to 24 hours. Reittmann's method of fixing in alcohol and 2 per cent. phosphotungstic acid and staining in warm carbol-fuchsin was found unsatisfactory.

In the material from chancres *Spirochæta pallida* was found in six of ten cases. In one case with four "sores" upon the prepuce *Spirochætæ pallidæ* were demonstrated in three of these "sores" two weeks before the appearance of the secondary eruption, and serum

from the fourth "sore" was not examined. In none of the chancres were *Spirochætae refringens* found.

Of the secondary lesions, examinations of the macules in two cases and of an erythematous eruption in one case were negative in several specimens. *Spirochæta pallida* and *Spirochæta refringens* were found in material from one mucous patch and from one moist sore on the scrotum. These five secondary lesions gave three negative and two positive results.

Of the three tertiary lesions — a gumma of the tongue, a tubercular lesion of the skin of the back, and a circinoid lesion of the palms — *Spirochæta pallida* was found only in the gumma of the tongue, with large numbers of *Spirochæta refringens*, and the congenital case was negative.

In seven cases inguinal glands were aspirated. Five cases, proved later to be syphilis, showed no *spirochætae* in the juice removed from the gland. Some of the material obtained from cutting the chancres showed a relation of the *spirochætae* to the red cells, described by Ploeger, in which the organism was found attached to red corpuscles. The *refringens* and the *pallida* in these nine cases, with the exception of the gumma of the tongue, were readily distinguished by their staining properties, by their size and by the number and distinction of their coils. In the specimens from the gumma of the tongue it was almost impossible to distinguish some *Sp. refringens* from *Sp. pallida*. There was absolutely no difficulty in distinguishing the other organisms. The serum from the œdematous prepuce in an early case of syphilis showed no *spirochætae*. The material from the case of vaginitis and from the amoebic dysentery stool contained also some large *Sp. refringens*, but nothing suggesting *Sp. pallida*. The serum from the chronic ulcer of the leg

contained many spirilla and fusiform bacilli. The material from the chancroids and herpetic eruption of the penis and from the psoriasis-like eruption of the forearm contained cocci or bacilli.

Discussion.

DR. SIMON FLEXNER said that he had had some experience in studying syphilitic lesions with reference to the occurrence of *Spirochæta pallida*. He thought it certain that the present methods of staining were unsatisfactory. There was one question of great importance which could not be settled until the staining technique was further improved, namely, when the examination should be considered negative. At the present the chief conditions almost, as far as the results go, would seem to be patience and the time devoted to the study of preparations. His assistant, Dr. Houghton, had studied specimens from the skin and internal organs of a case of congenital syphilis in which the skin lesions yielded the *Spirochæta* relatively easily, while the internal organs, on which several days were spent, yielded finally a single spiral of typical form in the liver. A longer search would probably have yielded still other occasional organisms, but no more time could conveniently be devoted to the search. Among the early specimens which Dr. Flexner had studied was the fluid from an inguinal gland. This fluid had shown, or it was supposed to have shown, the pallida in fresh preparations. The stained slides (Giemsa's solution) were at first negative, and the case was reported thus. Later, after more prolonged study, a small number of pallida were found in the stained specimens. Dr. Flexner was impressed in his studies with the rare occurrence of the coarser spirals—spirals of the refringens type. He

had seen a few individuals which might be regarded as intermediate or transitional forms between the pallida and refringens types, but they were hardly to be confounded with the former. It has been shown that monkeys and anthropoid apes are relatively easy to infect with syphilitic virus. Dr. Flexner's attention was early directed towards seeing whether the pallida could also be transmitted to monkeys. While his experiments were in progress Metchnikoff's findings were announced. However, the pallida was found by Dr. Flexner in the syphilitic lesion produced over the eye in a *Macacus Rhesus* by inoculation from a chancre. Kraus of Vienna had also confirmed this result and had followed the pallida to a second monkey inoculated from the first—in other words, in the second remove from the human disease. It was too early to say whether *Spirochæta pallida* is to be accepted as the cause of syphilis. In any case the discovery is an important one and will stimulate interest in this class of organisms. The occurrence of the pallida in secondary lesions of skin and mucous membranes, as well as in the primary syphilides, once its position is fixed, will render it easily accessible for purposes of diagnosis.

DR. CHARLES HERRMAN said that he thought it was not possible to say with absolute definiteness that this organism had or had not something to do with syphilis. Schaudinn had called attention to a group of organisms which was of great importance. He had not claimed that it was the cause of syphilis. With regard to the morphology, as Dr. Ewing had said, the transitional forms were very often present and the variation in the outlines was very great. He had been especially interested in the spirochætae which are present in the mouth normally and would like to ask Dr. Hastings what the

differential features were which enabled him to distinguish these organisms from the *Spirochaeta pallida*. It was very striking that the organism was found more especially in the lesions of the mouth. He asked what the conditions of the gums was in the cases treated with mercury. With regard to the number and depth of the coils that was a very variable quality. The same organism would be seen to have very deep coils in hanging drop and when stained the coils were not so numerous and not so deep. Probably this depended on the vitality of the organism and was not a point on which great stress could be laid. The thickness of the organism could not be taken as a differential feature. He would therefore like to ask what the differential features of the organisms were.

DR. EWING said that he agreed with Dr. Flexner as to the possibility of demonstrating single spirochaetae in an unlimited time. He had not been able to find them in some of his specimens in two to four hours. He believed, however, that if one looked long enough he would probably find a single *pallida* in practically all cases of syphilis.

DR. HASTINGS said in regard to organisms found in the mouth that he believed he had stated that it was not difficult to tell the difference between the *Spirochaeta pallida* and *refringens* and the *Spirillum* of Miller-Vincent. This was not a spirochaeta at all, apparently, and was easily differentiated by the fact that it is an organism which tapers at the ends, has only one or two loops, and occurs in large numbers with the fusiform bacillus. The case in which these three organisms were found was the gumma of the tongue. In the aspirated fluid only *pallida* and *refringens* were found. In the suspected gumma of the leg the only organisms found

were the Miller-Vincent spirillum and the fusiform bacillus. The difficulty was in differentiating the pallida and the refringens.

AN INTERESTING CASE OF RENAL DISEASE.

ALBERT A. EPSTEIN, M.D.

Dr. A. A. Epstein presented a rather interesting case of renal disease, with the following brief history. The patient was a man, sixty-two years of age, who had entered the hospital complaining of very frequent micturition. His history up to six years ago was practically negative. When a young man he had had an attack of gonorrhoea which was of short duration. He gave an indefinite history of having had kidney trouble in the last six years. Within the last three months the frequency of micturition had greatly increased, the amount at each time being very small. The patient could not recollect having at any time passed any blood or foreign body. Physical examination of the heart and lungs was practically negative. Examination of the bladder showed that it held only two ounces of fluid. The patient's urine was very fetid in odor; and bacteriological examination of it showed the presence of the *Bacillus proteus vulgaris*. A cystotomy was done on the patient to relieve the symptoms, two months after admission, with a fatal issue thirty hours later. A blood culture made six hours ante-mortem, on a variety of media, gave a negative result.

The autopsy was confined to a wound exploration, and only the kidneys and bladder were removed. The left kidney was found to be markedly hypertrophied.

The pelvis was distended and was filled with a fetid greenish pus. There were a number of miliary abscesses, both on the surface and within the substance of this kidney. The kidney measured eighteen by ten by five cm. An examination of the pus found in this kidney showed the presence of the *Bacillus proteus vulgaris*. The right kidney was small, measuring only three and one-half inches (8.5 cm.) in length. It consisted simply of a thin cortex and a pelvis. This kidney led into the ureter, which about an inch away from the cystic orifice, was plugged by a large calculus. About one and one-half to two inches from the pelvis of the kidney the ureter was stenosed. This was undoubtedly due to the stone having primarily been impacted at that point, producing a trauma which, after the passage of the stone further down, resulted in healing with stricture formation. The bladder was contracted and markedly trabeculated. It showed the presence of a rather severe cystitis. A small hemorrhagic polyp was present near the left angle of the trigone.

Discussion.

DR. E. LIBMAN called attention to a point which Dr. Epstein had inadvertently not mentioned. It was interesting to note that the stone absolutely prevented infection of the kidney, the inflammatory process involving only the bladder, the other ureter and the pelvis of the kidney of the opposite side.

AN UNUSUAL PEYER'S PATCH.

ALBERT A. EPSTEIN, M.D.

Dr. Epstein also showed a Peyer's patch of unusual length. It had been found at autopsy in the case of a child, six months of age, who died suddenly. From the autopsy findings a diagnosis of status lymphaticus with congenital narrowing of the aorta was made. The patch measured (without straightening out the folds of the intestine) twenty-eight cm., *i. e.*, eleven inches; but more accurate measuring after the straightening out of the folds showed its length to be thirty-two cm., *i. e.*, about thirteen inches.

Discussion.

DR. HARLOW BROOKS said that it appeared to him that the Peyer's patch was a very rare finding. He had never seen or read of one of so great size. He asked Dr. Epstein whether the diagnosis of status lymphaticus had been confirmed.

DR. EPSTEIN said that everything had pointed to that. The mesentery was one large mass of lymph nodes. On looking up the literature he had found that the largest on record was a patch reported by Ohlmacher. It was eleven cm. long.

OBSERVATIONS ON THE STAINING OF CAPSULES OF BACTERIA.

ALBERT A. EPSTEIN, M.D.

1. ON THE USE OF EGG ALBUMIN IN THE TECHNIQUE OF STAINING THE CAPSULES OF BACTERIA.

In view of the importance recently given to the study of the morphology of capsules in the differentiation of encapsulated bacteria,¹ a more general use of the methods devised for staining such organisms is not only desirable but necessary. The need of serum² in the preparation of specimens for the preservation and staining of capsules constitutes a drawback to a more general use of capsule stains where serum is not readily at hand. Egg albumin may be resorted to as a substitute for serum in such work. From a consideration of the chemical composition of serum, and by experimentation, Dr. Epstein had been able to determine that three elements are conducive to the preservation of the morphology of the capsule. These are: the presence of an albuminous material (in definite amounts); a certain amount of salt, and alkalinity. A menstruum can be made up from the white of egg which is in every respect as serviceable as serum in preparing specimens for capsule staining. The dilution of egg albumin, as determined by experiments on different organisms, which gives the best results is that of equal volumes of white of egg and distilled water. This is best done by adding to the white of one egg an equal amount of distilled water, shaking the mixture thoroughly, and preferably filtering it through cotton. This solution will keep for two weeks or longer without deteriorating. When greater definition of the outer

(1) Buerger. *Cent. f. Bakt., Bd. XXVIX, 1905, p. 335.*

(2) Hiss. *Cent. f. Bakt., Bd. XXVI, 1902, p. 302.*

portion of the capsules is desired, normal saline solution may be used in place of distilled water. Ordinary tap water may also be used. The additional alkalinity given by the tap water to the white of egg solution, serves to intensify the stain in general and to render it more diffuse, but does not interfere in any way with the form of the capsule. The organisms on which tests had so far been made were the *Streptococcus mucosus capsulatus*, the pneumococcus, and the *Bacillus mucosus capsulatus*. The staining was done by the Buerger method³ and in every instance a serum control was made. The results with egg albumin were not only satisfactory, but in many instances excelled those given by the serum control. In no instance did egg albumin fail to give a capsule where one had been obtained with serum; nor had any capsule been obtained with it where serum failed to give one. Further tests had been made of the application of egg albumin using the Hiss temporary and permanent methods of staining. The results with egg albumin were precisely the same as those obtained with serum controls.

2. REJUVENATION OF SPECIMENS.

. In studying comparatively the forms of the capsules of encapsulated bacteria, one finds that of the two methods of staining suggested by Hiss and Buerger; namely, the permanent and the temporary; the latter invariably gives a better result. There is a disadvantage in its use, however, in its not being at all enduring. It lasts at best, two or three weeks and then fades out completely. This difficulty may be removed and the method rendered much more lasting by a simple method of rejuvenation. The steps in the method are as follows:

(3) Buerger. *Medical News*, Vol. LXXXV, 1904, p. 1117.

1. Clear the cover slip of cedar oil and vaseline by means of xylol or benzine.
2. Wash the cover slip thoroughly in absolute or 95% alcohol for a minute or more.
3. Dry, restain, and mount as in the original methods⁴.

It is important to see that the washing in alcohol is thorough, for this step serves to remove all of the old stain and the remaining saline solution. The differentiation as well as the clearness of the resulting picture depends largely on this step. From a personal communication, Dr. Epstein had learned that Dr. Buerger had employed a similar method of rejuvenating specimens with like success.

3. MOUNTING OF SPECIMENS.

The use of vaseline in "ringing" or sealing the cover slips when mounted in potassium carbonate or sodium chloride solution, as suggested by Hiss and Buerger respectively, renders the specimens rather uncleanly, especially when they are used more than once. This too may be avoided by mounting the cover slips in the egg albumin solution suggested before. This facilitates the work considerably. Specimens so mounted keep for a few days at least. Dr. Libman had suggested sealing the specimens with Canada balsam or cement, after allowing them to dry for several hours.

Discussion.

DR. P. H. HISS said that Dr. Epstein's remarks on the use of albumin and on his experience with distilled and tap water, were very interesting. He had no doubt

(4) Buerger. *Medical News*, Vol. LXXVI, 1904, p. 1117.
Hiss. *Cent. f. Bakt., Bd. XXXI*, 1902, p. 302.

that Dr. Epstein knew that Boni had suggested some time ago a mixture of glycerine and egg albumin in about equal parts to which, to preserve this fluid, he added a few drops of formalin. Dr. Hiss had experimented with this particular mixture some years ago but had been under the impression that the pictures showed a so-called retraction zone rather than a true capsule staining. Even in the specimens shown this evening he found that instead of the capsule taking the stain there was an indication of an unstained space with the capsule apparently going into solution around the periphery of this. Of course, the same picture was obtained in a great many capsule stains. Dr. Wadsworth had used this half dilution of egg albumin in water, had written it up, and was about to report on it. In regard to the permanent mounts, of course with potassium carbonate or with salt solution a better picture was obtained when they were kept in the salt solution. With the copper sulphate, however, he had never felt that the appearance in the sulphate solution was better than when they were mounted in balsam.

DR. E. LIBMAN said that he had watched Dr. Epstein's experiments with a great deal of interest. Dr. Epstein had used egg albumin with water instead of with glycerine. As a rule the results were the same, but often the capsule was more distinct. By the use of the egg albumin a more solidly staining capsule was shown.

DR. A. WADSWORTH said that about a year and a half ago he had adopted Boni's suggestion to use egg albumin and had worked with it. He could not get as good results with the egg albumin and water as with the albumin and salt solution in the staining of sputa. The mixture of egg albumin with the sputum was very difficult; diffusion did not take place as readily as with the

serum. Dr. Wood had suggested that salt solution be used and Dr. Wadsworth had obtained better results with staining sputa in that way; but none of the specimens gave as good results as with the undiluted blood serum recommended by Hiss. For the staining of pure cultures he got the best results with the pure egg albumin but in his experience there was no advantage in using egg albumin over the serum, and as serum was much more convenient in his work he had not adopted the procedure very extensively.

DR. F. C. WOOD said that in some work which he had done on the pneumococcus about a year ago, he had tried a mixture of egg albumin and physiological salt solution or distilled water, and had added sodium salicylate to it as a preservative, like the ordinary Mayer albumin used in paraffin work. This albumin mixture kept for a number of months. The results in his hands had been fairly satisfactory, using the Hiss staining methods with copper sulphate. Dr. Wood thought that in most cases when working with sputum he had got better results with serum than with egg albumin. It was, however, certainly convenient to be able to extemporize a mixture when chest- or beef-serum was not at hand.

DR. EPSTEIN said that the objection raised to the use of egg albumin in place of serum on the grounds that it gave a retraction zone, did not hold good, because with the Buerger method of staining that effect rarely occurred. Such an effect could not be attributed to the egg albumin for in employing other methods of staining similar effects occur with serum. The claim made that with egg albumin the rim of the capsule stained more intensely than with serum might be answered by the fact that the intensity of staining does not depend on the albuminous substance present but on the degree of alka-

linity and the saline concentration of the solution used. The greater the alkalinity and the higher the saline concentration, the more intense is the resulting stain. A similar result might be obtained with serum which had been allowed to stand a long time so that all its ingredients had become concentrated and the alkalinity, as well as the saline concentration, heightened. Another effect of the heightened alkalinity was to render the outer edge of the capsule fuzzy in appearance, giving it a so-called mucoid character.

A CASE OF PRIMARY CARCINOMA OF THE APPENDIX.

RICHARD WEIL, M.D.

Dr. Richard Weil presented a specimen of primary carcinoma of the appendix, on account of the rarity of the condition. The patient was a man twenty-two years of age who had been sick a little over two months, the symptoms being due probably to the metastases rather than to the primary carcinoma. He entered the hospital at the end of August with considerable distension of the abdomen. He was very much emaciated and had a slight cough. The abdomen was swollen and contained fluid. The blood count showed a very slight anemia. The red cell count was well up to five million and the white cells were eight thousand. The abdomen was punctured, and 600 c.c. of bloody fluid was withdrawn. Part was injected into guinea-pigs on the supposition that he might have tuberculosis of the peritoneum, but the result was negative. Subsequently the man was sub-

mitted to an exploratory laparotomy when it was seen that there were a large number of carcinomatous nodules throughout. He died shortly after. His temperature was never above normal except immediately after the operation. At autopsy it was found that there were an enormous number of subperitoneal metastases, but none in any of the viscera. Sections of the appendix showed that the whole organ was transformed into a carcinomatous mass. The type of new growth was mucoid carcinoma. The appendix had not changed its shape and was not adherent. The fluid in the abdomen at autopsy was not bloody.

Discussion.

DR. F. S. MANDLEBAUM said that at Mt. Sinai Hospital in the last six years they had five cases of primary carcinoma of the appendix. Three of these cases had been fully reported two years ago by Dr. Moschcowitz. Subsequently they had had two more cases. These were all cases sent to the laboratory from the operating room and the tumor was in every instance a small, well-defined, localized growth which was not discovered until the appendix was opened. In none of the cases were metastases found. None of these patients had returned to the hospital since operation for any further trouble. On looking up recently the statistics in the hospital, of carcinoma of the intestine, it was found that out of the total number of cases of primary carcinoma of the intestine, primary carcinoma of the appendix occurred in between five and six per cent. At the General Hospital in Vienna, in 40,000 autopsies they had found but two cases of primary carcinoma of the appendix, the autopsies being of all kinds. But at the present time, when the appendix is examined very carefully, the disease is not quite so

rare as it formerly was. Most of the cases have been reported in the past ten years, previous to that Dr. Mandlebaum did not know of any case. Three of their cases were adenocarcinoma and two of them were medullary carcinoma. They were all small, localized growths which did not cause any stenosis, except one, and that was in the tip of the organ. Dr. Moschcowitz had collected all the cases in a very full paper published in 1903. The results showing a percentage between five and six per cent. of all primary carcinomas of the intestine, proves that it is really not so great a rarity as was formerly imagined.

DR. E. MOSHCOWITZ said that a point of great interest was that primary carcinoma of the appendix had a better prognosis than a carcinoma situated in any other part of the body. He was aware of only one other fatal outcome in addition to that which had been presented by Dr. Weil. This case was reported in France in the course of the past year. The reason for this excellent prognosis probably lay in the fact that, owing to the anatomical peculiarity of the appendix, the drainage of the lumen was early interfered with, even when the new growth was very small, and the patient soon developed symptoms of appendicitis for which he had recourse to early operative measures.

DR. F. C. WOOD said that before deciding about the primary nature of the growth he would like to have Dr. Weil open the entire intestinal tract. While he had no doubt as to the primary nature of the tumor, yet he thought that in justice to himself Dr. Weil should search through the gut very carefully before making any definite statements as to the primary nature of a growth in the appendix.

DR. G. P. BIGGS said that it seemed to him that Dr.

Mandlebaum's statistics were very high. They were hardly to be taken as the general experience. Speaking of fatal cases, he recalled the case of a man of about twenty-two who had been operated on some years ago. The appendix was removed and there was nothing in its gross appearance to indicate new growth; but adenocarcinoma was found. He had heard only recently that the man died a year and a half later of the disease.

DR. H. HAYS said that at times it was very difficult to find a primary focus in cases of carcinoma of the peritoneum. In some of these cases, he thought, there might be a primary carcinoma of the appendix. The five cases of carcinoma of the appendix collected at Mt. Sinai Hospital were all proved to be carcinoma under the microscope, although in the majority a suspicion was aroused by the gross appearance. The cases are at times difficult to diagnose grossly. A chronic obliterating appendicitis might simulate carcinoma and *vice versa*. He thought that the large proportion of five cases of primary carcinoma of the appendix out of a total of ninety-six cases of carcinoma of the intestine, might be increased by microscopical examination of all appendices, especially the chronically diseased ones. Almost all the cases of carcinoma of the appendix have been discovered within the last six years. Dr. Moschowitz in his paper had collected twenty-one cases. Mt. Sinai had two more, and Dr. Weil's case made a total of twenty-four. All of these have been in persons under forty years of age. Five patients were under the age of twenty and four under thirty. So that a great many had occurred in young people, and that might be one of the reasons why the condition was not more often thought of. There was no reason to doubt that if more careful search were made more cases of carcinoma of the appendix would be discovered.

DR. WEIL, taking up Dr. Wood's suggestion first, said that it seemed to him that the appearance of the appendix was in itself sufficient evidence of the primary nature of the growth. In the fresh condition he had passed the entire intestine through his hands, and there had been no indication of any other growth. As to the frequency of the condition, their experience at the German Hospital had been in marked contrast to that at Mt. Sinai. There had been three cases in the last five years and all of these were massive tumors. They were all inoperative. As regarded finding the tumors by chance, he did not know whether that was due to excessive care in the search and examination of the appendix. They had never come across a tumor, or any other condition which they would be willing to call carcinoma, by chance. There were conditions found which one might consider beginning carcinoma.

A NEW METHOD OF PREPARING AGAR- AGAR MEDIA.

JOHN CANARY.

Diener in the Pathological Laboratory of the Mt. Sinai Hospital, N. Y.

The advantage of the method which I wish to give in this paper is the rapidity with which the filtration can be accomplished, the resultant medium being perfectly clear. I will describe the method as applied to the making of three liters of agar, the amount which I am usually accustomed to prepare at once.

Three liters of water (tap water will do) are allowed to boil for two minutes. The agar (20 grams to the liter

or more if desired) is cut into small pieces in this water, and the mixture is allowed to stand for 15 minutes. It is then put upon the fire, again boiled for a few minutes, and the meat extract, peptone and salt are successively added. By this time the agar is completely dissolved. The proportions of these to three liters of water are:

Meat extract,	. . .	12 grams,
Peptone,	. . .	30 "
Salt,	. . .	15 "

The peptone should be added slowly. After these ingredients have been added, 20 c.c. of normal sulphuric acid are added and the mixture is brought to a boil for one minute. It is then cooled down to 50° C. The whites of eight eggs are then added. If only two liters of agar are to be made six eggs should be used; for one liter the whites of three eggs. Before adding the whites of the eggs they are mixed up with about 20 c.c. of water. After adding the whites of the eggs to the medium the whole should be well shaken so that the egg is well distributed. The flask is then put into the steam sterilizer for two hours. After this the mixture is filtered through a layer of cotton which has been thoroughly soaked with hot water. In pouring from the flask one should hold back the egg as much as possible and pour simply the clear fluid. This is not difficult to do as the egg has usually coagulated into one large mass. The filtration of three liters can usually be accomplished in five minutes.

After titrating and finding that the medium is of the right titre (with this method the medium is usually 1 per cent. acid to phenolphthalein), the fluid is poured into 500 c.c. flasks and sterilized in the usual way for four days in order to throw down all possible precipitate. (Three days' sterilization or less will suffice if one is not particular about having an absolutely clear medium.)

Before tubing the medium it is again filtered through cotton. The resultant product is a perfectly clear medium of proper consistency.

Notes:

(1) If meat infusion is to be used the method is carried out in the same way as above described, except that no meat extract is added. The peptone, agar and salt are added directly to the meat infusion.

(2) In preparing the medium a flask should always be used which is at least one liter larger than the amount of medium to be made up. For making three liters of agar it is best to use a five liter flask. This allows the medium to be more easily poured for filtration.

(3) Hydrochloric acid can be used instead of sulphuric acid, but the precipitate later thrown down in the flasks is more abundant.

(4) The reaction of the finished medium, as mentioned above, is usually about 1 per cent. acid, the mixture before adding the egg and boiling usually being 1.3 to 1.5 per cent. acid. After adding the egg and boiling it usually becomes 0.3 per cent. less acid. One can, of course, if one fears that the mixture is not 1.3 to 1.5 per cent. acid (which is the best titre at which to boil the agar), titrate before boiling and add acid or alkali as the case may require.

(5) It is advisable to have the white of the egg as free from yolk as possible.

(6) A bit of curved wire in the bottom of the funnel will prevent the cotton from sagging into the stem of the funnel.

(7) If only one or two liters of agar are to be made the medium need be kept in the sterilizer only from one hour to one and one-half hours instead of two hours; even when three liters are to be made a shorter period than two hours often suffices.

This method of preparing agar has been in use in the laboratory for a year and has been found satisfactory.

A FEW OBSERVATIONS ON THE MENINGOCOCCUS AND ALLIED ORGANISMS FROM THE NASOPHARYNX.

E. K. DUNHAM, M.D.

Dr. E. K. Dunham said that in the course of some work on cerebrospinal meningitis undertaken for the Commission appointed by the Department of Health, it

had seemed desirable to make a comparative study of Gram negative diplococci found in the nasopharynx of patients with the disease as well as in individuals not suffering from that disease. A number of such cultures were obtained, but whether among them there were any meningococci was a difficult question to answer. Cultures from the nose and throat fell into five groups. Of these four were very easily distinguished from cultures of the meningococcus by the appearance of the growth on 2 per cent. glucose agar, their characters being quite different from those of the meningococcus. The one group remaining it was very difficult to distinguish from the meningococcus; the variations in the meningococcus being so considerable that some of the cultures from the nose appeared identical with some from the spinal fluid. Among the cultures in this group there were six which were recognized as similar to the cultures provisionally designated as Catarrhalis. Cultural methods seeming so inconclusive in distinguishing between these different cultures, their relative susceptibility to agglutination was studied, the macroscopic method being employed. The chief difficulty was that of obtaining a serum at all specific. Sera from rabbits, geese, a goat and a horse were all tried; but the degree of dilution at which agglutination could be obtained was pretty low and direct comparison was rather unsatisfactory. Another difficulty in applying this method was the failure of many of the nose and throat cultures to give good suspensions in salt solutions. He then tried absorbing the specific agglutinins from the sera by using the different cultures for this purpose. Here great difficulty was experienced in getting the sera free of organisms and clear. Centrifugalizing the mixture of organisms and immune sera was tried; but it was very difficult to throw down the organisms, and

impossible to get a serum which was clear enough. Recourse was then had to filtration, but the results there were also rather unsatisfactory because the rate of filtration was so different with different cultures. Some would filter rapidly and some slowly. In some cases 40 to 50 c.c. would pass through a Berkefeld filter in a couple of hours; in other cases this would take twenty-four hours. In order to test the influence of obstruction of the filter, a colloidal solution of 1 per cent. boiled starch was used to dilute the serum in order to get a mixture which would filter slowly. This took out the agglutinins about as well as cultures exhibiting slow filtration. From this experience Dr. Dunham thought the method of filtration was open to suspicion. As far as the method of absorption of agglutinins was concerned, Dr. Dunham thought the results were not absolutely convincing. It seemed to him that a better method of distinguishing cultures was by the glucose fermentation test. In applying that he had used a medium composed of sheep serum with dextrose and bouillon and had found that all the meningococcus cultures obtained produced an acid reaction in this medium within twenty-four hours, which the next twenty-four hours might increase slightly. In no case did they produce any coagulation; whereas other organisms from the throat and nose about which he was in doubt, either did coagulate the serum with the production of acid or else produced an alkaline reaction.

Out of 172 cultures from the nose and throat, 15 had been studied quite carefully, and of these nine had produced just the change that was obtained with the meningococcus in this medium. As far as the agglutination tests could be considered as evidence, they also were in harmony with the results obtained with the cultures from the spinal fluid. Dr. Dunham thought that the reason

he had obtained so few positive results from the noses and throats of cases of meningitis was that the material had been delayed in reaching him, not that the organism was rarely present.

Discussion.

DR. A. WADSWORTH asked whether any of these cultures from the throat which resembled closely the meningococcus were found in any lesions, or whether any pathological activities had been noted in these closely allied organisms.

DR. DUNHAM said so far as the patients went usually there was very little if any inflammatory condition in the throat. As far as the animals were concerned they had been unable to obtain any lesions by inoculating them with these organisms.

DR. WADSWORTH asked whether they were found in lesions of cases dying of meningitis or other diseases.

DR. DUNHAM said they were not. The Gram negative diplococci which were probably not meningococci were usually much more virulent than meningococci from the spinal fluid. He had injected into a goose enormous quantities of meningococci without producing any local lesions and without markedly affecting the condition of the goose, whereas with Gram negative diplococci from the nose and throat which were not meningococci; it was very difficult to keep the goose alive during a sufficient period for immunization. The micro-organisms were much more virulent.

DR. W. H. PARK said that among the interesting points brought out by Dr. Dunham there were two upon which he would like to touch. First, an interesting point about the reading of the agglutinations. Some of the serum used by Dr. Dunham was also used in the Re-

search Laboratory of the Health Department. Dr. Dunham had kindly taken one of the cultures from that laboratory to test it by his method. Dr. Goodwin had obtained with the culture and serum observed in the hanging drop after three hours a complete reaction 1-80. Dr. Dunham, using the same culture and serum and employing the macroscopic method after allowing twenty-four hours in the ice chest, got a good reaction 1-2,000; that is, making the readings 20 times as high. One not noting the difference in the methods would be astonished in comparing the two readings. The reactions obtained with the cultures by either method could readily be compared together. Speaking of the cultural reaction as possibly more decisive than the agglutination, Dr. Park referred to two cultures Dr. Goodwin had obtained, as leading to an interesting speculation. Of the very many meningococci obtained from cords and cultures from the nasal secretion of those sick with meningitis or in contact with meningitis, all agglutinated practically alike; some in higher dilutions than others; but there seemed to be no qualitative differences. Cultures were made from fifty medical students. Diplococci obtained from two of these in cultural reactions and in their gross agglutinations appeared to be similar to the meningococcus obtained from meningitis cases; but when absorption methods were tried these two did not absorb the specific agglutinins from animals injected with cord cultures. They therefore undoubtedly differed from the cord cultures in their specific agglutinable substance. In animals, when injected into the spinal canal, they were pathogenic. These students were not in contact with meningitis. It seemed that as all the cultures from the epidemic cases whether from the nasal cavity or from the cord were in their agglutination characteristics qualitatively alike

though quantitatively different, and as these two cultures were qualitatively different, these did not belong to the type of meningococci exciting the present epidemic. The results of the starch experiment certainly necessitated that caution be used in ascribing absence of agglutinins in the filtrate to absorption by bacteria. As pointed out by Dr. Dunham, some bacteria probably hold back agglutinins more than others. When the agglutinins do pass into the filtrate as happens in most cases, the starch experiment would not be applicable.

DR. DUMHAM, in regard to the use of starch, said that the meningococcus cultures especially were very slow in filtering; the meningococcus producing a sort of slime very much as did the starch. He had tried this experiment with starch simply to use some colloid material that would filter as slowly as the meningococcus suspensions in serum. One culture from the throat, which was certainly not meningococcus, filtered just as slowly as any of the meningococci when used for absorption tests. This culture also removed the agglutinins for meningococci so that this result and that of the starch experiment are in harmony.

A CASE OF CARCINOMA OF THE BILE DUCTS AND DUODENUM.

J. C. A. GERSTER, M.D.

This case of carcinoma of the bile ducts and duodenum shows several points of interest. A brief abstract of the history is as follows:— Mrs. K. aged sixty-one years, a widow for seven years, was first seen by Dr.

Vineberg on August 1. She had suffered for several years from hemorrhoids and, during the past six months, had lost considerable flesh and complained of vague epigastric pain. On August 8, an operation for hemorrhoids was performed and at this time examination of the pelvis and abdomen under narcosis proved negative. After an uninterrupted recovery the patient was discharged on August 18.

On September 8, Dr. Vineberg was again called in and the patient stated that shortly after leaving the hospital she had again suffered from vague abdominal pain, now more pronounced in the right loin and back, accompanied by malaise and constipation. Three days before, on September 5, jaundice and clay colored stools were noted. At the time of examination she was deeply jaundiced, the urine was very dark, and the stools were light yellow in color. Deep palpation revealed a hard resisting mass in the gall-bladder region, firmly fixed, and not very sensitive. The diagnosis was made of stone in the common duct or malignant growth occluding the duct. On September 11, cholecystectomy was performed and a gall-bladder of moderate size, somewhat distended with a thick dark bile and many small calculi, was found. Probing showed the common duct to be patent. A hard mass was felt behind the duodenum at the junction of its first and second portions. The cystic duct was drained and the operation was completed in the usual manner. The patient died twenty-two hours afterward, apparently from shock.

Only an examination through the wound was permitted. The body was very adipose and deeply jaundiced. The peritoneum showed small areas of fat necrosis on the transverse mesocolon. The gastric mucosa was injected. The duodenum showed an ulcerated spot, $\frac{3}{4}$ cm.

in diameter, situated half way between the pylorus and the papilla of Vater on the posterior aspect of the gut; its edges were everted, undermined and somewhat indurated. Its floor was part of the periphery of a hard, ill-defined mass, 3 cm. in diameter, lying behind the duodenum and in front of the hilum of the right kidney. This tumor lay mainly to the outer side of the bile ducts which it involved at a point where the hepatic and cystic join to form the common bile duct. Here the mucosa of the bile passages was hard and white, and there was some stenosis, above the point of involvement the ducts were dilated and hemorrhagic; below it, the common duct was negative. The pancreatic and accessory pancreatic ducts were also negative. The pancreas showed a spot of injection at the neck but was otherwise negative to gross inspection. The right lobe of the liver was deeply bile stained up to the attachment of the falciform ligament. Sectioning showed a fatty liver with spots of acute necrosis. The other organs showed nothing of interest with regard to this case.

Microscopical sections showed the following conditions:—A section of the duodenal ulcer and its underlying tumor revealed a mass of fibrous tissue infiltrated with many small metastases of adenocarcinoma lying behind the intestinal mucosa, which at one point showed a dense surface growth of carcinoma. A section of the cystic duct including the hard white mucosa and the hemorrhagic part above it, showed a surface growth of carcinoma with underlying tissue dotted with metastases, while above this there was marked inflammation with necrosis. The liver showed marked acute degeneration with necrosis, Gram positive bacilli, fatty degeneration, pigmentation, and metastatic adenocarcinoma. Sections of the pancreas showed chronic interstitial inflammation, endarteritis, fat necrosis, and areas of acute inflammation.

Because both the duodenum and the bile passages showed areas of surface growth with underlying metastases, it was a question as to where the tumor was primary. Since the lesser pancreatic duct apparently led into the tumor, it also seemed a question as to whether the new growth might not have originated in the papilla of Santorini. Dr. Opie was kind enough to examine the specimen, and he considered that the idea of the involvement of the accessory duct could be excluded. After examining the microscopical sections, Dr. Mandlebaum thought the general type and arrangement of the growth appeared to suggest that the origin was rather in the mucosa of the duodenum than in the epithelium of the duct. Dr. Opie considered that it was impossible to say definitely where the growth began primarily, but thought the cells were of the character of those he had seen in other cases of cancer of the bile passages.

With regard to frequency, it might be said that according to Rolleston¹, carcinoma of the duodenum following an ulcer is of rare occurrence, whereas carcinoma of the extrahepatic bile ducts seemed to occur with marked frequency at the junction of the cystic, hepatic, and common bile ducts², which was involved in this case. This would tend toward the probability of the primary growth originating in the bile ducts.

In the matter of gall-stones being present in carcinoma of the bile ducts, Rolleston³ seemed to consider their presence the exceptions rather than the rule. In this case small calculi were found in the gall-bladder at the time of operation. The question of carcinoma aris-

(1) Rolleston and Trevor. *Journal of Pathology and Bacteriology*, August, 1905, p. 424.

(2) Rolleston, H. D. *Diseases of Liver*, 1905, p. 685.

(3) Rolleston, H. D. *Diseases of Liver*, 1905, p. 684.

ing from Brunner's glands can be excluded here because no adenomatous change in them was visible.

I wish to thank Dr. Mandlebaum and Dr. Opie for their kindness in examining the specimens and giving their opinions.

A PECULIAR FORM OF CELL NECROSIS OCCURRING IN THE LIVER.

HORST OERTEL, M.D.

Dr. Horst Oertel presented some observations which he had made during the past two years on a peculiar form of cell necrosis occurring in the liver. He had primarily regarded this as a curiosity; but the occurrence of other cases seemed to warrant for it more attention. The first observation concerned an individual who was admitted to the City Hospital in October, 1903, as a case of alcoholism. He had been on a debauch for three or four months without developing actual delirium tremens, but was in a very poor physical and mental condition. An additional clinical diagnosis of catarrhal jaundice was made. For two or three days he showed no additional symptoms though the jaundice got a little more marked. Then he suddenly developed what appeared to be an acute attack of delirium tremens, ultimately collapsed and died. At the autopsy there was found, besides the jaundice, a peculiar affection of the liver. The organ itself was large; it weighed about 1770 grams. It was dark yellow in color throughout, and perfectly smooth. On section the consistency was decidedly firm and leathery. The cut surface was pale but distinctly yellow. Scat-

tered through it were well marked but very irregular areas of deep congestion and apparent stasis, but the latter was irregular and not at all of uniform distribution. Deeper yellow to brownish yellow points or dots were scattered through the organ. There was no thrombosis of the portal vein and the bile ducts were free. The gall-bladder was free and contained fluid bile. The intestines and the stomach showed only chronic enteritis and gastritis. There was nothing of importance in the rest of the autopsy. It was difficult to make a gross diagnosis. Dr. Oertel had thought at the time of a peculiar form of cirrhosis, because such irregular cirrheses sometimes occur, though there was no evidence of growth of connective tissue. Microscopical sections showed a peculiar picture. Such a section presented a very irregularly stained appearance which was due to the fact that certain parts had retained their staining quality and others had lost it. In that way a peculiar pale streaky appearance was produced, which looked almost like a case of necrosis or pus formation. On microscopical examination that was not the case, however. The pale portions represented wasted area of liver tissue which was not the ordinary parenchymatous degeneration but a simple solution of individual liver cells which had taken place to a very pronounced and extensive degree. The starting point of the process was a simple fading of the protoplasm followed later by a similar change in the nucleus. The cells became paler and paler, but simply showed a moderate swelling and no granular disintegration. The outline of the cell was retained to the last and ultimately there appeared only a very faint reticulum, the protoplasm of the cell having been absolutely dissolved. During the process the cells developed larger and smaller vacuoles containing either fat or

bile. The picture which the completely degenerated area showed was very characteristic, so that one could distinguish it at a glance from the ordinary necrosis. There remained only a reticulum of the liver cells. Associated with it was a very pronounced stasis, which however was not uniform. Certain parts were perfectly free from it. The same applied to the bile imbibition. In certain spots this was very marked. Of great interest in that connection was the fact that evidences of inflammatory reaction were absolutely absent. The whole process showed itself as of absolutely passive nature. There was one point which attracted attention and that was a very marked involvement of the portal spaces. In this particular case the portal spaces were immensely thickened and this was especially marked around the portal vein, while the cellular proliferation was less marked and a good deal more recent around the bile ducts. In that connection it was very important to record that the thickening of the portal spaces was absolutely confined to them. No attempt was made to invade the liver tissue itself. Dr. Oertel at the time had shown this unusual finding to Dr. Ewing who discussed with him whether it should be called necrosis or not. Dr. Oertel had called it necrosis on account of the general marked tissue destruction; Dr. Ewing thought, however, that it was plain that these cells did not undergo what is ordinarily understood as necrosis of cells. Later Dr. Oertel had discussed the case with Dr. Adami. In the latter's opinion the process might represent a cytolytic one. In favor of that view was the fact that there was almost entire absence of any inflammatory reaction. Post mortem changes could be absolutely excluded on account of the lesion itself and the fact that the autopsy was done nine hours after death. Dr. Oertel had placed the case on

record as a curiosity and waited for further observations. About a year later a case was admitted to the City Hospital, originally as a case of emphysema with chronic bronchitis. While the first case had been a young man of thirty-three, this second was a man of fifty. It was noticed that he was a little stupid when admitted; he did not answer questions properly. He was slightly jaundiced. His dyspnoea during the next three or four days became quite marked and the attending physician had about 300 c.c. of blood removed. He improved somewhat but very soon went down very rapidly and became semi-comatose. His temperature rose to 101 to 102°; he developed delirium, and died five days after admission. In this case it was suspected that the disease might be the same as that observed formerly. On that account the house physician asked immediately for an autopsy, which was made one and one-half hours after death. Among other things there was found a liver of about normal size, perhaps slightly smaller, with localized thickening of the capsule, mottled surface, smooth and firm. On section it showed a marginal area spotted with irregular vascular injections. Toward the centre the markings were lost and the organ presented the same yellow spots. It was of a peculiar firm consistency. The microscopical sections showed exactly the same conditions as the first case. No similar changes were observed in any other organ. Dr. Oertel had exactly the same record of two other cases, one in a young colored girl of twenty-eight years who died of mitral stenosis, death being the immediate result of an operation, the other in a man of about sixty, who died of an extensive infarct of the heart. Within the last month he had observed a fifth case which he believed represented a very early stage of the process, in which he had been able to demonstrate

the first points of this peculiar cellular disintegration. It was of course known that the liver cells showed a very distinct reticulum even under normal conditions. What was observed in the cells showing the very early change was that this reticulum became more pronounced, while the portions of protoplasm which lay between this more prominent reticulum became fainter, until they actually disappeared. The reticulum became then more and more contracted and retracted, while the cellular outline was still preserved. Ultimately all the cell contents disappeared and left an open space which might contain fat and occasionally bile. A point of interest in connection with this bile imbibition was that there were two kinds; one in which large vacuoles appeared within the disintegrating liver cells and contained a large clump of bile. This had all the appearance of an active part of the cell. Second, the occurrence of small bile granules diffusely scattered over the disintegrating protoplasm. This appeared to be a passive process. It was impossible to find in the literature any record of similar or related cases. At the time the first case was studied Dr. Oertel had made a careful search for reports of non-inflammatory destructions of the liver. He had found one observation by Curschmann in which such non-inflammatory destructions of a multiple character occurred in the liver of decrepit individuals after long continued bile stasis. There was extensive breaking down of liver tissue which was not inflammatory. Curschmann was not able to give any evidences of the actual cellular change because in his cases the process had extended over a long period. It would perhaps be thought that in these cases the bile imbibition might stand in a certain relation to the process; but observation and comparison did not bear this out, because there was in each individual a

marked variation in the bile imbibition while the cellular waste occurred prominently in all. The change was most pronounced around the central vein, but was not confined to that. In one case it was more pronounced at the periphery. Whatever this change was it was different from the ordinary parenchymatous degeneration or the ordinary coagulation necrosis. It did not present granular degeneration nor the formation of structureless masses of protoplasm. On the other hand, the outline and appearance of the cell remained and the protoplasm simply dissolved. Dr. Oertel knew no better name than cytolysis. He had reported these cases rather early on account of the general interest now attached to the question of cytolysis and autolysis. It would be extremely interesting if some observations were to be made on the morphology of autolysis and especially to determine what pathological and clinical bearing such observations might have. The fact that within two and a half years five cases had been observed which were well defined made him believe that the condition might be more common than ordinarily supposed. Cases now grouped as parenchymatous degeneration and irregular stasis might belong to this category. However, there were many points to be cleared up. With regard to fatty changes, it would be interesting to see what fat was present, and what chemical changes accompanied this destruction of the liver.

Discussion.

DR. CHARLES NORRIS asked in what solution Dr. Oertel had preserved the livers, and also what the condition of the nuclei was in the cells which he spoke of as undergoing necrosis. He had not seen the sections, but from the descriptions he thought that some of the chan-

ges might resemble some of the early stages of what is called acute yellow atrophy.

DR. OERTEL said that the preservative used was the one ordinarily used at the laboratory, that is, formalin. The sections were put into formalin right after autopsy and left there for twenty-four hours. With regard to the nuclear changes it was interesting to note that the nucleus was attacked a good deal later than the protoplasm was, which conforms to practically all sorts of degenerative changes. The center of the nucleus showed the changes first. The nuclear chromatic remnants were scattered at the periphery and ultimately the whole thing simply became hazy and disappeared. Dr. Oertel fully appreciated the remark about acute yellow atrophy because that was considered at the very first and discussed in his first paper on the subject; but in any degeneration, as far as he knew, there was not an actual simple solution of the protoplasm from the very start, but granular disintegration with early loss of definite cellular outline. Later on there were secondary changes such as congestion. The process here was a distinctly individual cellular process. The protoplasm did not undergo any granular degeneration. There was, further, no formation of masses of dead protoplasmic substance as in necrosis, but simply a disappearance or solution; that is, a cytolysis. The appearance of acute yellow atrophy in the cases he had seen was much more violent even in the later stages. In early acute yellow atrophy there were distinct features of granular degeneration and coagulation necrosis, rapidly followed by the formation of fibrous tissue, spreading by very active cellular proliferation into the lost lobules. These cases showed nothing of that sort.

DR. NORRIS asked whether Dr. Oertel had used paraffin or celloidin sections.

DR. OERTEL said that he had used celloidin sections.

DR. F. C. WOOD asked whether any examination had been made of the urine of these cases for amino bodies.

DR. OERTEL said that no examinations had been made although he thought that such examinations would be very important. Waldvogel had made some observations on the occurrence of jecorin and protagon in cases of destruction of the liver. He considered that one could distinguish between livers containing jecorin and protagon by their color, one being yellow and the other brown. Waldvogel's observations had been made on cases of acute yellow atrophy and liver autolysis. (*Deut. Arch. f. klin. Med., Bd. LXXXII, 1905, p. 437*).

DR. HARLOW BROOKS said that he had been struck by the clinical picture of the disease. It seemed to him very much like the cases called Weil's disease, but the morphological changes were different, since in Weil's disease a true parenchymatous degeneration was found and in Dr. Oertel's specimens that was not so. He was free to confess that he had never seen anything just like it and was sure that no technical error was responsible for the lesions. Perhaps he had seen it and had never noticed it.

FIVE CASES OF PRIMARY CARCINOMA OF THE APPENDIX.

F. S. MANDLEBAUM, M.D.

Dr. F. S. Mandlebaum said that in discussing Dr. Weil's case of primary carcinoma at the last meeting of the Society, he had made the statement that at Mt. Sinai Hospital during the past four years he had had the op-

portunity of examining five cases of primary carcinoma of the appendix, and had also made some remarks concerning the frequency of this condition taken from the Hospital statistics. In closing the discussion, Dr. Weil had unintentionally cast some doubt on the diagnosis of these cases and Dr. Mandlebaum had felt it his duty to bring them before the Society. Unfortunately, the gross specimens were no longer accessible, but slides and photomicrographs of all the cases were shown. All of the specimens had been removed in the operating room and sent to the laboratory for diagnosis. The clinical histories in each instance had pointed to an acute or chronic appendicitis, and in no case was any suspicion of a malignant growth aroused before operation. It was only after section of the organ that the tumor was seen. In four of the cases the tumor was easily recognized grossly but the malignant nature even then was suspected in only two of the cases. The tumors ranged from four millimeters in diameter to thirteen by seven millimeters. In one case the growth was somewhat diffuse and its measurements rather uncertain, but in the four other cases the tumor was sharply defined. Three of these cases had been fully reported by Dr. A. V. Moschcowitz in the *Annals of Surgery* for June, 1903. Since that time there had been two additional cases at the hospital. There were many points of interest in connection with this subject, but Dr. Mandlebaum wished simply to say a few words regarding diagnosis and frequency. In reference to the diagnosis of these five cases, one could not possibly have made any other diagnosis than carcinoma. The cases of chronic inflammation with cell proliferation mentioned by Dr. Weil, did not come into consideration in the present series. The usual type of adenocarcinoma was seen as a rule; but in one case the picture was more

like a medullary carcinoma. A tendency to proliferation was noted in most instances; and at some distance from the main part of the tumor in some of the sections the pictures resembled a scirrhus of the breast. In some of the cases nests of tumor cells were found in the deep longitudinal muscle fibers, the circular layer of fibers being left entirely free.

It might not be out of place to mention certain changes that frequently occur in the sympathetic nerve plexuses of the appendix as well as of the intestines proper, that might give rise to some difficulty in diagnosis. At times, both in acute and chronic diseases, the proliferation of ganglion cells in Auerbach's plexus is so marked that it might cause an impression of the presence of a tumor, naturally of a metastatic nature. This point had been brought out by Askanazy some years ago, in a paper before the German Pathological Society, on the behavior of ganglion cells in peritonitis. For some years Dr. Mandlebaum had noted these changes; and not only in peritonitis but in other conditions as well, he had noted a considerable involvement of Auerbach's plexus. These changes were quite interesting in connection with this subject, and Dr. Mandlebaum presented several photomicrographs showing the lesions. The slides were taken from the collection of recent cases, such as chronic enteritis, polypoid colitis, acute appendicitis, and enterocolitis. Some cases showed proliferation of the ganglion cells, leucocytic infiltration of the muscle fibers, as well as dilatation of the peri-ganglionic lymph spaces. The last named condition was found in a case of entero-colitis accompanied by a marked congestion of the entire gut with probable lymph stasis. Meissner's plexus might be affected in a similar manner. Errors might thus arise, but could hardly be made by an experienced observer.

In regard to the frequency of primary carcinoma of the appendix, Dr. Mandlebaum said that during the past twelve years they had examined at the Mt. Sinai Hospital ninety-six cases of primary carcinoma of the intestine; five of these were primary in the appendix, making 5.2 per cent. These cases constituted three-fourths of one per cent. of carcinoma from all sources. That these figures were not high when careful systematic examinations of all specimens was made was seen on comparing them with figures given in a paper by Dr. L. K. Baldauf of the Bender Laboratory, in the December number of the *Albany Medical Annals*, 1905. In the Albany Hospital, five hundred and twenty-one examinations of diseased appendices had been made. Five cases of primary carcinoma had been found, that is, about one per cent. Three of these cases form the basis of the paper and in two of these no tumor could be seen on gross examination. This observation alone would corroborate the statement made by Dr. Hays at the previous meeting, that more cases would be discovered if more care were taken in the examination of the material. At the Mt. Sinai Hospital, during the past four years, eight hundred and eighty-eight cases of appendicitis had been operated upon, but not all of the specimens had been sectioned, as in many instances a gross examination was all that seemed necessary to establish the diagnosis. All specimens showing an unusual appearance were examined histologically. From these cases the five cases of primary carcinoma were obtained, making somewhat over one-half of one per cent. of all cases operated upon.

Discussion.

DR. CHARLES NORRIS said that in a case of colloid carcinoma of the stomach which had been operated upon

at Bellevue Hospital there had been found a tumor of the appendix, as large as the little finger, which on microscopical examination revealed a colloid carcinoma similar to that in the stomach. He thought therefore that one should be a little careful in diagnosing primary carcinoma of the appendix. He supposed in many cases primary carcinoma of the appendix did occur, but it was hazardous to say that this was the original source. It was possible that the tumor might be primary in both situations.

DR. HARLOW BROOKS asked Dr. Mandlebaum if he had been able to trace the subsequent history of any of these cases, which would give some clue as to the prognosis of these tumors.

DR. MANDLEBAUM said that he had been very much tempted in preparing these case to go into other points besides the diagnosis and frequency, and more especially the question of prognosis. These cases dated back only to 1901, but inasmuch as three of them occurred in private patients he thought that if a recurrence up to the present time had happened he would have known of it. So far as he knew no cases have been reported in the literature in recent times in which metastatic deposits have been met with. All the cases had been primary and had never recurred. He had one other case which he had not included in this series because although he felt perfectly satisfied that the case was a primary carcinoma of the appendix, the condition of the slide was such that he had hesitated about showing it. He was perfectly willing to defend the diagnosis on the other five cases. The sixth case presented a small lymph node in the mesentery of the appendix which was very much involved, and there were strands of carcinomatous cells coming down from the mucosa, which, however, were not seen in the section. Consequently he had not exhibited

the specimen. Those shown under the microscope, however, showed the beginning of the process from the mucosa of the organ and the extension downwards.

DR. E. LIBMAN said that one of the cases presented by Dr. Mandlebaum had been a patient of Dr. Goodman, who could perhaps give the subsequent history.

DR. A. L. GOODMAN said that there had been no evidences of any recurrence. The case had been diagnosed as ordinary catarrhal appendicitis. At the operation a small enlargement of the tip of the appendix was found and on examination the diagnosis of carcinoma was made. There was no history of carcinoma in any relative of the family.

DR. BROOKS asked how long ago the operation had been performed.

DR. GOODMAN said that it was two years ago.

NEGRI BODIES, WITH SPECIAL REFERENCE TO DIAGNOSIS.

ANNA W. WILLIAMS, M.D.

The history of the findings in hydrophobia is rather instructive. Up to 1903, notwithstanding much painstaking work on the lesions in this disease by many of our most eminent pathologists, certain bodies, described then for the first time by Negri (possibly seen before by one other recording observer), were entirely overlooked. And what makes it more interesting is the fact that these bodies with the methods now in use come out with such startling distinctness and individuality that even the beginner in studies on the nervous system can not miss seeing them.

In the Research Laboratory of the Health Department, Dr. Poor has corroborated the work of others in regard to the presence and specific nature of these bodies in fixed and stained sections from the nerve centers in cases of rabies, and, for some time, he has used the section method for diagnosis. By this method, however, it is impossible to make the diagnosis before twenty-four hours, and no one so far as known has published a much shorter way of demonstrating the bodies satisfactorily.

In connection with a report made by Dr. Poor before this Society 1904, the writer demonstrated a smear from hydrophobia brain tissue containing these Negri bodies, and recommended the smear method for rapid diagnosis. Smears were made and studied at that time at the suggestion of Dr. Ewing, who as we all know had obtained such good results by this method in his studies on ganglion cells. By the technic then employed, though the Negri bodies were brought out clearly, they were delicately stained and their differentiation from the surrounding tissues, especially from the red blood cells, was somewhat difficult.

Recently the work has been taken up by us again, and it has been found that by slightly improved technic and a different stain the bodies in most instances, if not in all, are brought out more distinctly and more characteristically, and can be identified in a much shorter time and by much simpler and less expensive technic than by any other method so far published. The work has been controlled on one side by Dr. Poor's section cuttings and animal inoculations, and on the other side by the writer's smears from the central nervous systems of normal animals and of animals that have died from tetanus, diphtheria and meningitis; and it seems reasonable to make the positive statement that the bodies seen in smears as

well as those seen in sections are specific to hydrophobia. Further, the smear work seems to have brought out more clearly than the section work with us that these bodies are not degeneration products; that is, that they have an individuality distinct from the nervous tissue. This is shown by the fact that they are definitely and regularly structured according to the age of the lesion, and this makes it more probable than ever that they are living organisms belonging to the group of Protozoa and that they are the active cause of hydrophobia.

The technic is as follows: The nerve tissue is obtained as soon as possible after the death of the animal (though smears made by Dr. Van Gieson as late as ten days after death have shown bodies stained well enough for diagnosis). Smears may be made in any way that will get the tissue quickly and evenly on the slide. However, with the help of valuable suggestions given by Dr. Van Gieson we have found that the best results can be obtained by the following method.

The small bit of nerve tissue required for the examination is cut out with the point of a sharp scalpel and placed under a glass slide. A cover slip is put over the piece and pressed upon it gently until it is well spread out; then with the finger still pressing lightly the cover slip is moved slowly along to the end of the slide. It moves very easily and makes a thin, more or less evenly spread smear. The smears are allowed to dry in the air and are fixed either in Zenker's fluid or in methyl alcohol. Dr. Poor recommends Zenker and he has gotten some beautiful results with it followed by staining with eosin and methylene blue after the method of Mallory. So far methyl alcohol seems to be a better fixative for the Giemsa stain which the writer has used extensively in this work and which stains the bodies very character-

istically. The smears are fixed in methyl alcohol for five minutes, the dilute Giemsa stain is then poured on them while they are still moist with the alcohol, and left on from one-half an hour to twenty-four hours. About two hours seems to give the best results. After one-half hour, however, the bodies may be clearly identified. The stain is removed by washing in a stream of tap water; the smear is dipped into a mixture of equal parts of methyl alcohol and 50% ethyl alcohol for decolorization; and after washing again in tap water and drying with filter paper it is ready for microscopic examination.

The Giemsa stain used was prepared by Dr. Field, whom we wish to thank for his suggestions in regard to its use as well as for other helpful suggestions during this work.

The bodies vary in their stained appearance according to the time stained, the amount of decolorization, the thickness of the smear, the age of the lesion, and the length of the time after death. In the stage of the disease that is usually found in the so-called "street rabies", that is, in the stage which oftenest reaches us for diagnosis, most of the bodies, according to the Giemsa method of staining given above with the stain left on for one hour, stain a rather dark robin's egg blue, with purple granules or central body. With more decolorization the protoplasm is a clearer blue and the chromatic masses red. Many of the bodies by this method of staining show a double contour or membrane-like periphery which may be an artefact as it is more apparent in bodies within the cells and in the thicker parts of the smears.

The finer structure of these bodies will not be spoken of in detail at present; suffice it to say that the small rounded forms show a chromatin staining, ring-shaped, central body; the small oval forms may show

two or three such bodies. Some of the larger rounded forms show chromatin bodies arranged more or less regularly around the periphery as well as in the center; some of the large oval forms show a chromatin rounded body nearer one end with small chromatin granules irregularly scattered throughout the rest of the body.

The slide demonstrated by Dr. Poor shows some of these structures, and some of the other forms are shown in the other slides demonstrated. One of the slides demonstrated is from a calf that died from spinal meningitis. It is placed there to show the immense number of intact ganglion cells which may be obtained by the smear method. The smear was made from the floor of the fourth ventricle in the region of the nuclei of the hypoglossal, the glossopharyngeal, vagus and spinal accessory nerves.

Discussion.

DR. D. W. POOR said that he could only speak in corroboration of what Dr. Williams had said. It seemed to him that a very important advance had been made in the diagnosis of rabies by this improvement in the smear method. Dr. Williams had alluded to the importance of making a rapid diagnosis. Whereas by the old methods of sections it was possible to arrive at a diagnosis by the end of twenty-four hours, this was not the rule. In many cases it was delayed, sometimes two or three days. Some people, however severely they may have been bitten, are unwilling to commence treatment until they are sure that the animal which bit them was rabid. By this method one could arrive at a diagnosis in a very short time. This method also would probably give even better results than the sections, partly because the cells appeared to be better preserved and the morphology was more

perfect. In addition to the advantage of rapidity of diagnosis there was another. In all experimental work on rabies we have oftentimes animals inoculated with virus and owing to the long period of incubation and the irregular symptoms there was sometimes uncertainty whether the animals died of rabies or not. It would seem as though this difficulty had been cleared up and one could determine whether rabies was the cause of death or not without resorting to re-inoculation with the consequent delay of two weeks, or the slow method of sections with its troublesome technique. A very important point had been brought out by Dr. Van Gieson's method of making smears. Although the bodies could be recognized when separated from ganglion cells it was of advantage to have them in their natural position. By this method the cells were preserved intact. It was possible to have a slide covered with ganglion cells. Personally, Dr. Poor liked fixation in Zenker's solution and subsequent staining in eosin and methylene blue separately better than the combination stains. A sharper outline could be obtained.

DR. W. H. PARK spoke of the shortening of the time needed to make a diagnosis of rabies. The Pasteur treatment of persons bitten by rabid dogs had been undertaken by the Health Department about eight years ago. At that time, the method of detecting whether a dog had rabies was to inject a rabbit with material from the suspected animal. To make a diagnosis required anywhere from twelve days to three weeks. Dr. Wilson had suggested that guinea-pigs be used, and it had been found that these animals would give a diagnosis in half the time, and had the added advantage that they did not die from sepsis as readily as the rabbits. Then came the discovery of the Negri bodies. Brain tissue stained and examined in sections required but two days for diag-

nosis. Now, through the smear method devised by Dr. Williams, the time was still further cut down so as to be but about two hours. It was interesting to note here as in many other instances, that people widely separated happened to work out a discovery at about the same time. Just before the publication of Negri's report on these bodies had appeared, Dr. Williams and Dr. Poor had noted these bodies and were very much interested in their study and were endeavoring to discover whether they were specific for rabies.

DR. JAMES EWING said that he had had the pleasure of looking at some of the slides and wished to confirm all that had been said about the distinctness of these bodies and the ease of diagnosing the disease. He thought it would be well to mention that Dr. Poor and Dr. Williams had had considerable experience and that their results were better than a beginner could expect in his first efforts. So that if the first results were unsuccessful it should be recognized that the technique could be improved with practice. The ability to diagnose rabies by this method in such a short time was certainly a great step in advance. One of the most disgusting features about some laboratories was the constant assortment of rabid animals. The experimental production of rabies for diagnosis might now be discontinued. When Dr. Williams expressed her conviction that this method offered sufficient data to demonstrate the protozoon nature of these bodies, most of the members, Dr. Ewing thought, would hope that they might agree with her, but would perhaps think that some work was still necessary before that belief could be accepted. In regard to the luck of priority of which Dr. Park had spoken, Dr. Ewing suggested that while the discovery of these bodies was a very important event, perhaps the

demonstration of their nature would be a still more important one, the credit for which would overshadow the importance of their discovery.

PRELIMINARY COMMUNICATION UPON A SPIROCHÆTAL INFECTION OF WHITE RATS, AND OBSERVATIONS UPON THE MULTIPLICATION OF SPIROCHÆTAE IN FLUID MEDIUM.

CHARLES NORRIS, M.D.

Since our last communication to the Pathological Society, the spirochætae have been kept alive through a series of inoculation from rat to rat.

Without entering into a detailed description of our observations on the disease in white rats, the following statements may be made.

I. A subcutaneous inoculation in white rats, with blood containing spirochætae, is followed in the course of two or three days by the presence of more or less numerous spirochætae in the circulating blood. These persist from one to three days.

II. Unlike the spirochætal infection of man and monkeys, no relapses occur.

III. The rats show no obvious symptoms of illness, no local reaction, no visceral lesions of consequence, save turgescence and enlargement of the spleen.

IV. In all, a series of about twenty-five (25) generations have been kept alive through rats.

V. Observations show that immunity is conferred, 1) by previous infection; 2) by simultaneous inoculation

of spirochætal blood, plus small doses of serum from animals that have gone through a previous infection. For example, three monkeys that had gone through an infection with relapses, could not be again infected with spirochætal blood. Rats which have once been infected, also show complete immunity to further inoculation.

We have also determined that serum taken from monkeys that have recovered from the disease, when mixed with spirochætal blood, and injected simultaneously, retards or completely inhibits the development of the spirochætae in the circulating blood of rats. Serum from one of us, who had recovered from an attack of spirochætal fever, showed identical properties.

These observations are in accord with those made by Levaditi, with the spirochætae of the Brazilian fowl disease.

Subcutaneous inoculation of similar small doses of serum, followed several days later by injection of spirochætal blood, has not, in the few experiments made, prevented the development of the infection.

Similar doses of normal serum, either mixed with spirochætal blood, or administered before, does not prevent or retard the development of the infection in rats.

VI. Regarding the mode of reproduction of these organisms, we have seen nothing in the study either of fresh or stained specimens, to suggest that longitudinal division ever occurs. On the other hand, the constant occurrence of organisms showing an extreme attenuation in the central portion, as well as organisms lying end to end, with their pointed extremities in close approximation, strongly indicates transverse fission or possibly fragmentation.

Under certain conditions, which we do not under-

stand, long, thread-like forms are seen showing several areas of attenuation.

VII. We have seen no evidence of an enveloping or undulating membrane in specimens stained by Wright's, Giemsa's, Proscia's or Loeffler's methods.

We have likewise found no evidence of distinct cilia; unless the finely drawn out terminal portions constitute cilia. From the observation of hanging drops, we are under the impression that each end determines the corkscrew movement in one direction.

These observations lead us to infer that the spirochætae more closely resemble the bacteria than protozoa. In confirmation of this, we have never noted either in fresh or stained specimens, any chromatin particles. R. Koch, in the last number (47) of the *Deutsche med. Wochenschrift*, arrives at similar conclusions; and in his study of infected ticks, he has likewise failed to detect any transformation or change in the morphology of the spirochætae indicating a sexual cycle; as seen in various hemamoebae or trypanosomata.

VIII. *Cultivation Experiments.* After experimenting with a large number of media, of various compositions, we have obtained in several instances, positive evidence of the multiplication of the spirochætae in fluid media. In human and rat blood, to which has been added sodium citrate, to prevent coagulation, there can be seen within 24 hours after inoculation with a few drops of rat blood containing spirochætae, a very evident increase in the number of these organisms. By this we mean that, notwithstanding the dilution of several drops of infected blood with many times its volume, say 3 to 5 c.c. of medium, the spirochætae are vastly more numerous in smears from the culture fluid than in control smears taken at the time of inoculation.

Furthermore, by inoculating several drops of this first generation into a second blood tube, we have found the organisms in the transplant, but not so abundantly.

The third generations, however, have failed to grow, although in the hanging drop, non-motile, and in stained specimens, granular or moniliform organisms were seen.

We have reason to believe that our failure to obtain growths in the third generation may be due to variations existing in the human blood employed. We have hopes that with a more careful discrimination in the use of favorable blood, we may obtain growth through successive transplantations.

Multiplication likewise occurs in the undiluted citrate blood from infected rats, kept over night at room temperature. One of the specimens under the microscope shows the tangled clumps which have formed over night in such blood.

Worth recording, incidentally, is the fact that citrated rat blood, kept at room temperature for six days, retains unimpaired, its infective properties.

REPORT ON SPIROCHÆTE PALLIDA FOUND IN AN EARLY CASE OF EXTRA-GENITAL LUES.

H. S. HOUGHTON, M.D.

Dr. H. S. Houghton gave the results of some studies on the *Spirochæte pallida*, expressing his indebtedness to the staff of the City Hospital for the material upon which he wished to report. In order to bring out clearly the particular point of interest in this case, Dr. Houghton ran briefly over some recent developments in the work on *Spirochæte pallida*. Schaudinn, in a recent article, pointed out that while various spirochæta-like forms have

been found in various pathological processes as well as in cases of undoubted syphilis, the *pallida* as delimited by its proper morphological characteristics, has been found only in syphilitic products, and in them with great regularity. The characteristics which Schaudinn lays down for the identification of this organism are as follows:—

1. It must be a relatively long organism, with numerous (10 to 26) deep, regular spirals.
2. It must be of great tenuity.
3. It must react feebly to all stains.
4. It stains pink with the new Giemsa method, all other forms with the same stain coming out purple.
5. It must have tapering and pointed ends.

To this may be added that the *Spirochæte pallida* is probably a flagellate organism while other common forms, such as have been found in ulcerated carcinoma, in various non-luetic venereal lesions, and in the mouth, are non-flagellate, but possess a perfectly definite undulating membrane. Still more recent publications by Bandi and Simonelli, by Levaditi and Salmon, and by Volpino and Bovero, are of great importance, inasmuch as these observers have by a method of silver impregnation been able to bring out the organisms in sections and to study their distribution in various parts of the body.

The point of interest in this particular case was the possibility, in the event of this organism being positively proved to be the cause of the disease, of making a diagnosis in doubtful and in early cases. The patient was a young girl, a Scot, seventeen years of age, admitted to the City Hospital ten days before. There was nothing of special interest in her history; she had had no illnesses except an attack of measles in childhood. She denied venereal disease. She had been a prostitute for the past three months. Her present trouble had begun about two weeks before with the appearance of what she

called an ordinary "cold sore", which from the history she gave suggested a simple labial herpes. A small, red, soft area appeared on her lower lip which itched and was scratched open. From that time it had become progressively larger and more painful. A few days ago a hard, somewhat painful swelling had appeared under her chin.

Examination showed a round ulcer at the right inferior margin of the lower lip, 2.5 cm. in diameter. It was covered with a thick, hard, brownish crust, and on pressure a small amount of pus exuded at the side. The margin was slightly irregular, but there was practically no induration about the sore. The submental glands were large, very firm, and not very painful. There was no other apparent glandular enlargement, and nothing else was to be seen. Smears made from some of the pus and from curettings from the base of the ulcer showed large numbers of organisms which conformed in every particular to the characteristics laid down by Prof. Schaudinn. They were more abundant, however, in the blood obtained from the base of the sore; while in the pus there were, besides the *Spirochæte pallida*, some larger forms, possibly *Spirochæte refringens* or some of the mouth saprophytes.

This was the second case in which Dr. Houghton had seen a diagnosis made by this means, cases which were otherwise very dubious as far as clinical diagnosis could go.

Addendum: Examination of the case reported above, made on December 20, 1905, one week after report was made, showed an unmistakable maculo-papular rash over the chest, upper abdomen, and back. The lip lesion remained practically as noted above. The submental glands were exceedingly firm, and painless.

A PNEUMOCOCCUS PRODUCING A PECULIAR FORM OF HEMOLYSIS.

E. LIBMAN, M.D.

Dr. E. Libman presented for Dr. Epstein a pneumococcus which had a peculiar action on blood-plates. Dr. Libman said that last Spring he had shown the Society a streptococcus which produced a double ring of hemolysis around the colonies on blood-plates, his being the first observation of the kind as far as he knew.

The present organism was isolated by Dr. Epstein from the blood of a case of pneumonia on the fifth day of the disease, the sputum in the same case showing a typical pneumococcus which caused no hemolysis on blood-plates. The present organism was of interest in two connections. In the first place, pneumococci had not been found to cause any hemolysis on blood-plates, the organism generally growing green. In the second place, the hemolysis was of a peculiar type; next to the colony was a clear ring, surrounding this was a ring of somewhat darkened blood, outside of which there was again a clear ring. The organism fermented inulin, did not precipitate on serum-glucose-agar (within two days), and was possessed of the typical morphology and type capsule (Buerger).

The observation proved that it was necessary not to depend too much on hemolysis on blood-plates as a diagnostic sign. It was probable that the pneumococcus had developed this peculiarity because of having been in the blood, it having been noted previously that pneumococci from the blood current are apt to behave peculiarly.

Discussion.

DR. THOMAS FLOURNOY said that he could not remember ever having seen any pneumococcus or streptococcus which gave an appearance like this shown by Dr. Libman.

BASOCELLULAR AND PLANOCELLULAR CANCER OF THE TONGUE, SIDE BY SIDE.

W. N. BERKELEY, M.D.

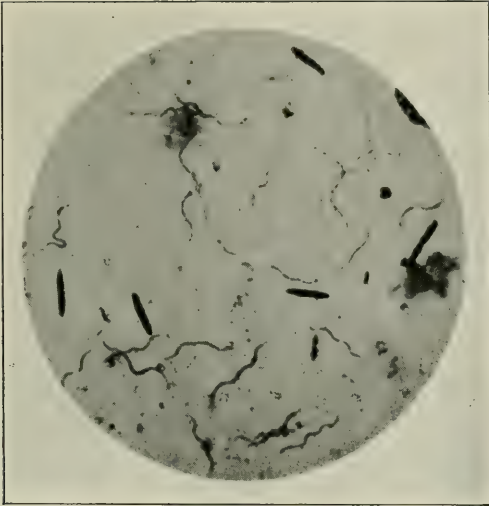
Dr. William N. Berkeley presented sections from a case of epithelioma of the tongue. The patient was a man of rather advanced years who had applied at the Presbyterian Hospital Dispensary for treatment for an indurated mass on the right edge of the tongue, on November 20 of last year. A microscopical diagnosis of typical epithelioma was made, there being a large number of cornified epithelial "nests" in the growth. A second piece was excised later. In the later sections, besides the first type of epithelioma and associated with it there was undoubtedly an additional growth. This was in all regards similar to the tumor which has received much attention in recent years and has been called basocellular cancer. Both growths were progressing actively side by side, and mitotic nuclei were abundant. Dr. Berkeley did not attempt to interpret this finding, but thought it worthy of attention.

A RAPID AND CERTAIN METHOD OF STAIN- ING SPIROCHÆTE PALLIDA.

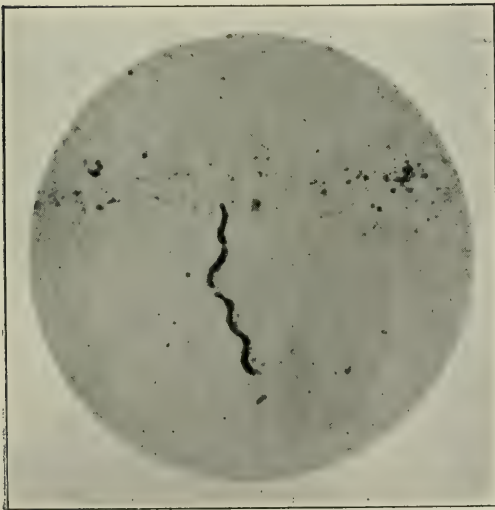
L. B. GOLDHORN.

Mr. L. B. Goldhorn said that he had had an opportunity of studying a number of cases of syphilitic lesions, some of which had been treated with mercury. These included four cases of primary lesions, eleven cases of secondary lesions, three cases of tertiary lesions, and four doubtful ones. By the staining method which he wished to describe he had succeeded in finding the Spirochæte

pallida in all undoubted cases of syphilis, except in tertiary lesions. The initial lesions were on the vulva, lip, and penis; secondary, one mucous patch in the corner of the mouth, four on the tongue, three on the pharynx, one roseolar rash on the arm, one on the chest, and one dry papule on the arm. Of the tertiary lesions, one was on the eye, one on the cheek, one on the arm. Of two doubtful lesions on the penis, one remained negative; one on the face and one on the leg also remained negative. It was doubtful whether these lesions were secondary or tertiary. Two cases of eczema and one of acne were examined, these remaining negative as regarded finding the pallida. Mr. Goldhorn considered the staining a relatively simple matter and readily accomplished with any of the chromatin dyes. Perhaps the results obtained by such stains as Wright's and Hastings' and the Nocht method were not as pretty as by the method to be described, which was also clearer. The dye was similar to the blood stain which he had described elsewhere, and was made as follows: Dissolve one gram of lithium carbonate in 200 c.c. of water and add two grams of methylene blue. Place in a double boiler and heat carefully until the polychrome has formed. Neutralize by taking one-half of the solution and acidifying it with 5 per cent. acetic acid, using litmus paper to determine this point, and immediately add the second half of the polychrome. Before being acidified the polychrome should be poured over cotton so as to remove the precipitate and then allowed to stand for a day. To this corrected polychrome is added a weak solution of eosin. The methylene blue should be preferably Merck's medicinal, though B X Grüber would serve. The French eosin (eosin rein) is used. The amount of eosin used could not be definitely stated, but it was added until the



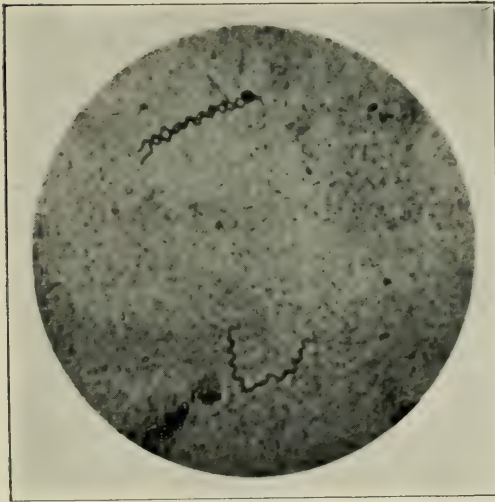
Sp. of Vincent.



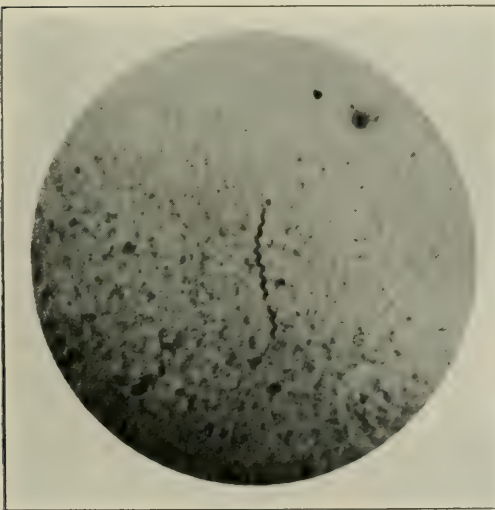
Sp. refringens.

filtrate was of a pale blue, watery color. The resulting precipitate was allowed to stand for a day or two before filtering. The precipitate was dried without heat and dissolved in commercial wood alcohol. The use of this commercial wood alcohol was preferable to the use of Merck's C. P. or Kahlbaum's. The commercial alcohol fixed much more quickly. The solution was again allowed to stand for some time, because of an insoluble residue which should be removed. It was then again filtered. Curiously enough it had been found that such dyes when allowed to stand in open vessels had a better action than dyes immediately put up in closed bottles. The solution made was very concentrated, almost saturated. Although it was impossible to say just how much acetic acid or eosin was used, one or two trials would put one on the right track, so that uniform results were obtained. The method of staining was extremely simple. The stain was dropped on to the unfixed preparation and left for a few seconds; the slide was then slowly placed in water film side down, and held in this position for four or five seconds so as to allow an interaction between the dye and the water to take place, and was then moved about in the water to wash it. It was then stood on end to drain and allowed to dry spontaneously or dried by waving it in air, without the use of filter paper or heat. The results obtained in this way were not really uniform. It seemed to make a difference whether the preparation came, for instance, from the mouth or from the genitals or from the arm. The different percentages of salts in the medium in which the parasites were contained seemed to be a factor in the rapid staining reaction, but staining of the pallida never failed to take place. The staining could be compared to that of the chromatin of the malarial parasite. One could stain the organism pale pink or

blackish blue, just as one could stain the nucleus of young malarial parasites pink or blackish blue. The saprophytes, which in some preparations were very confusing seeming to bear a resemblance to the pallida, were readily stained with an alkaline polychrome solution without the addition of eosin, but the pallida would not stain unless the eosin was added. Refringens also stained without the addition of eosin. As regards the number of pallida found, this varied greatly. In one specimen shown, twelve were seen in a single field. In another case, the arm roseolar, only one pallida was found after forty minutes search. If there were pus present it should be removed, though Mr. Goldhorn did not think that the leucocytes really interfered with the staining reaction; only few parasites are seen in the pus. In regard to the technique of obtaining the specimens, the curette was used to remove all surface epithelium and pus, and the appearance of a little lymph or blood was waited for. The slide was then touched to this and the smear made. If the patch were in the throat a platinum loop was used. In the fresh specimens the pallida had not been seen. As regards the morphology of the pallida, it showed as usual the characteristic sharp turns. It is thinner than practically all other organisms. The spirochæte found in one case of eczema had similar turns but was thicker. Flagella had been demonstrated several times on the pallida by Mr. Goldhorn. The body itself did not show any evidence of a membrane but it seemed to show a granule near the end. The other spiral organisms have an undulating membrane as described by Schaudinn, which can be made out with a powerful light, and stains bluish by this method. As far as the division of the parasite was concerned evidence of two flagella had been seen, and two parasites had been seen lying side by side,



Sp. pallida.



Sp. pallida.

the ends apparently welded together. Mr. Goldhorn drew attention to the leucocytes seen in the pus of secondary lesions. Some pus corpuscles seemed to show peculiar changes, for instance, a peculiar vacuole with faintly staining center, not seen in ordinary exudates. Moreover, there was one, possibly two forms, in these preparations stained for pallida which did not belong to the ordinary exudate. They were bodies one-fourth or one-sixth the size of red corpuscles. They showed a large number of granules, sometimes little chromatin granules peripherally. The second body was still smaller, the size of a blood platelet, with a distinct chromatin body in its center. The pallida had been found not infrequently straight, in places showing a few turns at one end or at the middle.

Discussion.

DR. HARLOW BROOKS said that the preparations of Mr. Goldhorn's which he had examined were very much more satisfactory than any others he had seen. Not only was the method very quick but it was very clear.

TWO CASES OF GLANDERS.

A. M. PAPPENHEIMER, M.D.

Dr. A. M. Pappenheimer reported on two cases of glanders observed at Bellevue Hospital. The first case was a man, fifty-five years of age, a stableman, who was admitted April 4 to the service of Dr. Lusk. He was delirious when admitted and no history regarding the mode of infection could be obtained. His condition on admission was as follows: Well developed, well nourished man; skin hot and dry; scarred on forehead; spastic con-

dition of right arm; delirious; tongue dry and coated; pulse rapid. The patient showed every sign of a severe systemic infection. Examination of the heart, lungs, liver, spleen, etc., was negative. After admission he became rapidly worse and there was developed a swelling on the right shoulder and down the arm, over which the skin was red and shiny. On the scalp there was an indurated wound, the center of which was ulcerated and the edges undermined. After the second day a pustular rash developed over the body. He had a number of convulsions before death, which occurred on the fifth day after admission. The temperature ranged from 102° to 105°. The urine was negative. Blood counts showed a slight leucocytosis, 10,000, with 80 per cent. of polymorphonuclears. Blood cultures showed a number of raised, whitish colonies, about 100 to a plate. Morphologically these were small Gram negative rods with the characteristics of the glanders bacillus. Smears and cultures were made from the pustule on the forehead and the glanders bacillus was obtained. Emulsions were injected into a guinea-pig and after two days produced characteristic inflammation.

The autopsy findings were as follows: Scalp showed a central defect and around this an area four inches across with small elevations, 1 mm. to 1 cm., with yellow heads. Similar pustules were seen in the right eyelid, the left cheek, and the neck. There was a large pustule over the lower edge of the sternum containing brownish pus. Pustules were also scattered over the abdomen and there was an abscess on the right forearm and muscles of various parts of the body. The abscesses all contained thick brownish pus. Under the abscess over the lower end of the sternum the bone was eroded. The skin of the scalp showed a number of typical farcy

buds on the pericranium. The entire cellular tissue of scalp was the seat of multiple abscesses. The heart showed nothing abnormal. The lungs showed adhesions over the right lung and in the pleura and scattered through the lung were small yellowish foci. The tonsils were enlarged greatly and exuded pus on section. On the posterior wall of the larynx and elsewhere there were a number of foci with yellowish centers. The other organs showed no lesions of consequence. At the autopsy streak plates were made from the heart's blood and from the pus about the shoulder joint; from these the glanders bacillus was recovered in pure culture.

In the second case, the patient, also a stableman, was infected directly from a horse with the disease. The exact manner was not determined, though the man had an open wound on the right thigh and may have been inoculated through this. There were no symptoms for three weeks, a very long period of incubation. At that time he suddenly noticed a sharp pain in the left side and a few hours later had a severe chill. The onset of the disease was just like that of lobar pneumonia. Examination on admission showed a well developed man, apparently acutely ill; skin hot and respiration rapid; signs of pleurisy over the left lower lobe. He had no cutaneous eruptions. During the following twelve days he ran a high temperature, 102 to 104.5°, a temperature very typical of typhoid or acute general miliary tuberculosis. The tongue was dry, pulse became weaker, respirations increased. Blood examinations showed a slight leucocytosis, 13,000 to 15,000, rising just before death to 19,000. No cutaneous eruptions appeared during his illness, but about three days before death a number of deep seated nodular swellings were noticed scattered over the trunk and limbs. The skin over these was perfectly normal.

About this time swelling of the right hand and right knee joint was noticed, with marked tenderness. Blood cultures showed about thirty-five colonies of glanders bacilli to each plate. Blood flasks showed a mucoid flocculent sediment and hanging drops showed chains of short bacilli. Subcultures on potato showed characteristic brown viscous growth. Postmortem examination showed the external appearance as described. Nodules were scattered over all the body, more extensively on the right arm, on section situated deep in the subcutaneous tissue or in the muscles themselves. The pus was thick and brownish. The hyperaemic zone which was very conspicuous in the first was not at all marked in the second. The knee joint and the joints of the right hand contained pus. The left lung over a portion of the lower lobe showed thickening of the pleura and a number of superficial abscesses which proved to be glanders abscesses. The liver, spleen, and heart were negative. The larynx showed oedema and on the anterior wall there was a group of small submucous abscesses which contained thick pus. There was no inflammatory reaction about these. The other organs showed no interesting changes. Smears from the abscesses and cultures from the spleen showed the glanders bacillus. A guinea-pig was injected with a broth suspension of pus from which the glanders bacillus was obtained in pure culture. The guinea-pig showed slight swelling of the testicle. Three days after injection it was autopsied and a number of small abscesses were found about the seminal vesicles and tunica vaginalis. The testicles were swollen to about twice the normal size. The characteristic things in the histological picture were emphasized: 1. The absence of any marked reactive inflammation about the individual nodules except for the hyperaemia; the mass of

necrotic cells was sharply demarcated from the adjacent tissue. 2. The karyolysis in the nuclei of the necrotic cells. This change is said by Orth to be particularly marked in glanders though it occurs in other diseases. The tonsil was interesting as it showed marked involvement. In the first case this may have been the portal of entry.

STENOSIS OF THE AORTA AT THE JUNCTURE OF THE ISTHMUS.

A. M. PAPPENHEIMER, M.D.

Dr. A. M. Pappenheimer presented a case of stenosis of the aorta at the juncture of the isthmus, which had been unsuspected during life, as are most of these cases, and was accidentally found at autopsy. The patient's family and previous history were negative except that he had had rheumatism. Of the present illness only a few facts were learned. He was admitted to the Skin and Cancer Hospital, before coming to Bellevue, because of swelling of the abdomen. A diagnosis of tuberculous peritonitis was made and laparotomy was performed, but he grew steadily worse. Physical examination on entering Bellevue showed a general petechial eruption. There was pulsation of the carotids. The left hand was cold and of a purplish color. There was no pulse in the left radial artery because of thrombosis of the left brachial artery. The femoral pulses were barely palpable, the popliteal absent. There were no superficial pulsating arteries about the thorax. The heart showed a double murmur at the base and was moderately hypertrophied. There was a high leucocytosis and marked anaemia with increase of polymorphonuclears. The au-

topsy showed a markedly emaciated man; general purpuric rash; oedema of the feet; petechial blotches over the intestinal serosa. The anterior mediastinal glands were enlarged and tuberculous. The liver was cirrhotic, and there was marked ascites. The heart was very interesting. The aortic valve showed only two valves, and at the juncture there was considerable nodular thickening. There was acute endocarditis and fresh vegetations on the ventricular wall. The foramen ovale was closed. The ascending and transverse aorta were of normal caliber. Just below the subclavian the aorta was thrown up into a ridge and the lumen was moderately constricted. There was a smaller, more shallow ridge towards the posterior wall. About two cm. further down, the aortic wall was thrown up into a very marked ridge and there was a marked constriction at this point. The lumen of the aorta was very small. The appearance was that of a fibrous diaphragm which partly occluded the aorta. The internal mammaries and the deep epigastrics were greatly dilated. The internal mammaries were as big as the finger. The details of the collateral circulation were not studied. In addition to these lesions the patient had a lobular pneumonia and infarcts of the lungs.

The stenosis at the isthmus was not a great pathological rarity. Series of cases had been collected by several observers. In all there have been about one hundred and sixty cases reported, one hundred and five in adults, fifty-five in new born children. Clinically it was improbable that the stenosis at this point ever caused marked symptoms. The condition develops slowly, offering time for the establishment of a compensating collateral circulation. Diagnosis had been made during life in some cases in spite of the absence of any marked subjective circulatory disturbances. The diagnosis was based

on the fact that the pulsation in the femorals and lower extremities is greatly diminished as contrasted with the radials and carotids. In general there are two types of stenosis; one occurring in children and due probably to a simple persistence of the narrowing which is normally present at birth. The stenosis in new born children appears as a gradual, funnel-shaped constriction. On the other hand there is a type which is met with in adults and which the specimen shown partly represents. Just below or at the entrance of the ductus arteriosus, less often a little above it, the wall of the aorta is thrown out so as to form a diaphragm. It seemed as if a ligature were placed around it at this point. The specimens showed a double stenosis. Just a little below the subclavian the aorta was folded up; then there was a slight diminution in the caliber of the aorta until the ductus arteriosus was reached, and three mm. below this point there was a very tight stenosis, only four mm. in diameter. The ductus in this case was closed. Still another type is seen, a very rare congenital anomaly, atresia of the aorta at this point.

The causation of the condition has been the subject of considerable theorizing and has been attributed entirely to an arrested development. Others lay emphasis on the contraction of the ductus arteriosus, the fibers of which are continuous with the aortic wall. The variation in the site is explained by the variation in the angle at which the ductus enters the artery and the variation in the amount of connective tissue about the ductus. One other theory, that the stenosis is due to the organization of a thrombus formed during the obliteration of the ductus arteriosus, has received but little attention.

Discussion.

DR. T. C. JANEWAY said that Dr. Pappenheimer had not mentioned whether there was hypertrophy of the left ventricle.

DR. PAPPENHEIMER said there was a moderate hypertrophy of the left ventricle, due to the associated aortic insufficiency.

DR. E. LIBMAN said that this type of congenital lesion was perhaps second in interest. He had been struck with the fact that the isthmus varied greatly in size in different specimens, and thought that it would be of some importance to determine the normal size of the isthmus at different ages. He had seen cases which he could explain only by there having been a certain amount of narrowing at the isthmus, not sufficient to class them as cases of stenosis proper. Dr. Libman had shown a specimen before the Society two years ago in which there was marked stenosis in a man of sixty-three. Death in that case was due to the development of arterio-sclerosis in the collateral circulation and to the formation of a large ridge of atheromatous tissue in front of the isthmus. He said that he thought that a certain grade of narrowing was responsible for some cases of atheroma confined to the ascending arch of the aorta, and that the same lesion might be responsible for some cases of otherwise unexplained hypertrophy of the left ventricle. In the case which Dr. Libman had shown there was a distinct dilatation of the aorta beyond the stenosis. He had not seen Dr. Pappenheimer's specimen yet, and would therefore like to ask whether such a dilatation was evident in it.

DR. PAPPENHEIMER said that in his case there seemed to be a slight dilatation beyond the stenosis.

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DR. F. S. MANDLEBAUM, *President.*

THE CONSTITUENT OF THE BILE CAUSING PANCREATITIS AND THE EFFECT OF COLLOIDS UPON ITS ACTION.

SIMON FLEXNER, M.D.

It has been proved by Opie that a diversion of the biliary secretion into the pancreatic duct causes pancreatitis. This paper is believed to show the constituent of the bile which causes the inflammation, and the mechan-

ism by which the injurious action of this constituent may be modified and controlled.

Bile contains two sets of constituents, crystalline principles, including biliary salts and coloring matter, and colloids, chiefly nuclealbumin. The bile salts act injuriously upon various cells, the other constituents are not known to be cellucidal. Injection of a solution of bile salts into the pancreas of dogs causes acute pancreatitis; while injection of the muciginous constituents causes no inflammation. Injection of the two bile constituents re-combined causes less severe inflammation than does the salt constituent alone. This inhibitive action of the alcohol-insoluble constituents of the bile may be due either to some substance antagonistic to the action of the salts, or to the physical properties of the medium restraining the injurious action of the salts. Experiments where the colloid strength of the bile is increased by adding a bland colloid substance, prove that the injurious activity of the bile salts is restrained, chronic instead of acute lesions appearing. When the colloid strength is diminished by the addition of saline solution, the injurious activity of the biliary salts is unchecked. A colloid suspension, if enough is injected, may itself act as a foreign obstructive body and so cause sclerotic lesions of the pancreas. But the loss of biliary coloring matter in a colloid suspension of bile constituents shows that an interchange of fluid occurs between the gland and the suspension. Upon the rate of this diffusion and consequent degree of concentration of the biliary salts in contact with the parenchyma of the gland, depends, probably, the extent of the lesions. When a colloidal substance is used which is incapable of congealing in the ducts and is not readily reduced in density by pancreatic digestion, it protects the pancreas against the

poisonous biliary salts; the reactions may be reduced in severity or even entirely prevented.

In human pathology a condition simulating the experimental one is found when an obstruction of the ducts causes the well known loss of diffusible salts, and inflammation an increase in muciginous constituents. Such a modified bile might, on entering the pancreas, set up subacute or chronic lesions. These experiments may serve to account for certain heretofore unexplained instances of partial or independent sclerosis of the pancreas.

THE ISOLATION OF THE MENINGOCOCCUS FROM A CASE OF SCARLET FEVER.

AUGUSTUS WADSWORTH, M.D.

The presence of pathogenic bacteria in scarlet fever and its sequelæ has of late been so extensively studied and the pyogenic cocci, particularly the streptococci¹, have been so frequently found, that the presence of a micro-organism hitherto not associated with scarlet fever may be of interest.

This micro-organism was isolated from the exudate of a knee joint synovitis developing in one of several cases of scarlet fever which broke out in the wards of the Nursery and Child's Hospital, New York. The first cases of this epidemic clinically were obscure, but as the disease developed and other more typical cases appeared, the diagnosis was finally established. The clinical history of the case, for which I am indebted to Dr. Rowland G.

(1) For complete bibliography see JOCHMANN, *Zeit. f. klin. Med.*, 1905, Bd. LVI, p. 315.

Freeman, has been abstracted to show the type of the disease and the special points of interest.

On May 19, 1901, this child, a boy aged two years nine months, developed suddenly a temperature of 103.4° , green stools, a congested and swollen throat, and an erythematous rash on the trunk and extremities. The temperature fell to 100° on the 20th, and the rash faded. On the 21st a macular rash covered the entire body. By the 24th this had faded. The urine was normal. Desquamation appeared on the 30th, and the urine, of a specific gravity of 1.010, showed a trace of albumin on the 31st. On June 1st, the temperature again rose, reaching 105.6 on the 3d. After a bath it fell temporarily to normal; it was 103.6 on the 6th. June 7th, swelling, redness, and tenderness were noted over the left first metacarpophalangeal joint, slight redness and tenderness over the right fifth metacarpophalangeal joint. The urine, of a specific gravity of 1.009, showed a heavy trace of albumin, and the temperature was 99° . On the 8th, both hands were edematous and an effusion with pain developed in the right knee joint which, though tender, was not red. The temperature was 101.2° on this day and the next. On June 11th, the temperature reached 104° ; the knee joint was swollen, somewhat tender, but not red; the skin was desquamating in large patches; large white patches were seen at the angle of the mouth, the signs of a beginning angina; the urine showed a heavy trace of albumin; the specific gravity was 1.008. On the 12th, the temperature fell to 100.6° , but again rose, reaching 104.6° on the 13th. On June 18th, the mouth and lips were greatly swollen. The swelling of the knee had diminished slightly, but it again became tender and swollen on the 24th. The temperature was elevated and continued high, ranging between 101° and 104° until the child's death on July 5.

At the autopsy, Dr. David Bovaird made the anatomical diagnosis of Cancrum oris, Bronchopneumonia, Hydropericardium, Suppurative Synovitis of the right knee. The knee was swollen and contained a thick exudate like the white of an egg with a yellowish red tinge.

Bacterial examinations of the exudate in the knee were made three weeks and five weeks after the beginning of the scarlet fever. The second examination failed to reveal the presence of bacteria. The first examination showed cocci, singly and in pairs, outside and inside the cells, as many as twenty-eight were found in a cell. These decolorized by the Gram method of staining.

On June 11th, two cubic centimeters of a clear, straw colored, viscous fluid, containing mucous shreds and flocculi, were drawn with considerable difficulty under aseptic precautions from the right knee joint. A portion, about 0.5 c.c., diluted with broth, was injected into the peritoneum of a guinea-pig and under the skin of a mouse. The animals recovered rapidly from the inoculation and there were no signs of infection apparent. The remainder of the exudate was studied in smear and culture. The microscope failed to reveal any micro-organisms in the clearer, more fluid portions of the exudate, but in the thick shreds and flocculi, leucocytes and cocci were found with the methyl blue and Gram methods of staining. The cocci for the most part decolorized, but a few retained the anilin gentian violet¹. These were similar morphologically to the cocci which decolorized. A few of the leucocytes contained considerable numbers of these decolorizing cocci usually grouped in pairs. No capsules could be demonstrated although the retraction

(1) It was found that the mucus interfered with the alcohol decolorization of the Gram procedure. After longer exposure to the alcohol very few cells retaining the gentian violet were found.

zone about each cell was marked. The single cells were spherical, those in pairs were bean shaped. Tetrads were found, but no chains. In short, the cocci showed the morphology and grouping of the gonococcus.

Cultural studies of this exudate were made under aerobic and anaerobic conditions, in meat infusion and meat extract media—broth and agar with and without glucose, glycerine agar, coagulated glycerine serum tubes, and in media to which fluid ascitic serum had been added. With the exception of one tube all these cultures failed to show any growth even after two weeks observation. After seventy-two hours incubation at 37° C., one tube of glucose agar which previously had been carefully boiled to expel all the oxygen, showed a zone of white colonies, pin point in size, lying 1 cm. below the surface of the agar; in short, just such an appearance as has been considered typical of anaerobic growth. In subcultures, however, the organism proved to be strongly aerobic and it was found that this appearance of anaerobism was due to the lodging at that level of the tube, of a viscous shred which offered the only favorable conditions for growth. The morphology, staining reactions, and grouping of the cocci found in these colonies corresponded to those found in the smears of the exudate. In the first subcultures there were even a few which decolorized with difficulty by the Gram method. The division of the cells apparently took place in two planes.

By means of smears on the surface of neutral meat infusion agar diluted with fluid ascites serum, subcultures were obtained, but on no other media,¹ whether aerobic or anaerobic, did any growth appear. In this first sub-

(1) Aside from the usual laboratory media with and without glucose or lactose, deep tubes of glucose serum agar free from oxygen as well as coagulated serum tubes with glycerine or glucose were tried.

culture the colonies developed slowly, attaining the size of a pin head after forty-eight hours incubation. Under the microscope they resembled the colonies formed by gonococci; namely, of a gray white translucency with coarse central granulation and homogeneous or very finely granular periphery, the border even and sharp, and the whole colony comparatively flat. After repeated transfer in subcultures the growth of this micro-organism became more luxuriant on the serum agar plates until cultures were finally secured on a specially prepared meat infusion agar. From this, growth was rapidly secured in agar, gelatin, and broth made from meat infusion. Finally, it was coaxed to grow, though poorly, on meat extract media.

The surface growth of this micro-organism on agar was flat, translucent, whitish in color, becoming brownish with age, and of a slimy, stringy consistency like the cultures of *B. Friedlander*. In punctures, the growth was slight and confined to the upper portions of the tube. Under strictly anaerobic conditions the organism did not develop even in the most favorable media. Growth in the presence of lactose failed to give any evidence that this sugar was split or used in the cell metabolism.¹ As little growth took place at the room temperature, cultures in gelatin with and without fluid ascites serum were

(1) At the time this organism was isolated, the carbohydrate fermentations of the meningococci and allied organisms had not been worked out in extenso, nor have they since proved essential in the differentiation of these species. With the older methods, no acid was produced in lactose litmus agar, and no gas in glucose media, although glucose had proved a valuable addition to the media in securing the first cultures from the exudate. The more delicate methods of determining the carbohydrate reactions suggested by HISS (*Jour. Exp. Med.*, 1905, Vol. VI., p. 317; 1905, Vol. VII, p. 547), for other species of bacteria and used by DUNHAM (*Proceedings of this Society*, 1905, N. S., Vol. V, p. 134), in his study of the meningococcus, were not then in general use.

incubated for several days and cooled to determine the liquefaction of the gelatin. On cooling, such tubes were always solid. In broth and fluid ascites serum, the growth took the form of thin flakes, or a pellicle floating on the surface, and these from time to time settled to the bottom of the tube. The grouping in broth was that of a micrococcus, the cell division being in two planes. Very few chains were seen, and these were always short, consisting of not more than four or five cells. Tetrad grouping was seen in these cultures. The coccus was apparently non-motile.

Five cubic centimeters of a serum gelatin culture of this coccus were injected into the peritoneum of a guinea-pig; smaller quantities into the ankle joint of a rabbit, and into the cornea of a guinea-pig. The pig inoculated in the peritoneum was extremely sick and was expected to die for three days after the injection, but it then made a rapid recovery. The other animals quickly recovered from the inoculation.

The agglutination action of the patient's blood serum on this coccus was tested in hanging drop. As only a few drops of the patient's blood could be secured it was impossible to study the reaction macroscopically. In dilutions of 1-1, as compared with controls of human sera, definite reactions appeared in the hanging drop after a few minutes observation. Owing to spontaneous agglutination and the great susceptibility of this organism to any change of medium, be it serum or broth, the results obtained in higher dilutions were considered uncertain.

On June 25, a second specimen was obtained from the knee joint of this child. The appearance of the exudate was the same as that secured previously, but no micro-organisms were found in either smear or culture.

At the same time swabs from the mouth and throat of this patient and also from three other children recovering from the same epidemic were carefully studied without again securing cultures of this micro-organism, but in the smears cocci were found which decolorized by the staining method of Gram.¹ At the same time these specimens were obtained, the child from whose knee the coccus was isolated had a well marked angina and the other cases were convalescent. The large number of bacteria present in the specimens and the predominating numbers of streptococci and staphylococci rendered the isolation of an organism so extremely sensitive to a change of environment as this coccus, practically hopeless even if it had been present.

Owing to the comparatively few biological characters shown by this organism and the lack of reliable differential standards among organisms of this class, the identification of this micrococcus was considered in a measure uncertain. For purposes of comparison cultures of known stocks of the gonococcus, the meningococcus, and the *Micrococcus catarrhalis* were obtained from Dr. E. Libman. The catarrhal coccus was easily differentiated. The gonococcus, similar in morphology, grouping, staining reactions, and colony formation, was only eliminated by its failure to grow on artificial media to which no fluid serum had been added. From the meningococcus the micro-organism isolated from the knee joint of this case of scarlet fever could not be differentiated by any known test.

(1) A few of these decolorizing organisms were isolated. The cultures, however, failed to correspond with the organism obtained in the knee. Attempts were made to identify some of these species with the decolorizing cocci described by other observers, notably CLASS (*Phil. Med. Jour.*, 1899, Vol. III, p. 1066) and WEAVER (*Amer. Medicine*, 1903, Vol. V, p. 609); but the standards for comparison were indefinite and the results were considered uncertain.

In conclusion it may be noted that this micrococcus in its morphology, its reaction to the Gram stain, its presence within the cells of the exudate from which it was isolated, and, finally, in its biological peculiarities shown by growth on media,¹ corresponds in every particular with the meningococcus. I have withheld reporting these results in the hope that recent study in extenso of the meningococcus would reveal the existence of closely allied pathogenic forms and thus guard against error in the identification of this organism. As these studies have substantiated the previous methods of identification, and as there has as yet been described no other species of pathogenic bacteria exhibiting these characters,² this organism may reasonably be considered to be a meningococcus.

Attention may also be directed to the fact that an organism which was secured in culture with such great difficulty from uncontaminated exudate, might easily be overlooked in the examination of material containing other bacteria as is so frequently the case in scarlet fever. It is in this light that I have reported the case without attempting to draw any inferences as to the significance of the findings.

Discussion.

DR. THOMAS FLOURNOY said that at Bellevue within the last year they had been using various sorts of serum water media in attempting to differentiate the meningococcus from other similar cocci. In working with menin-

(1) Vide, WEICHSELBAUM, *Fort. d. Medicin*, 1887, Bd V, pp. 573, 620; *Cent. f. Bakt.*, 1902, Bd. XXXIII, p. 510; ALBRECHT AND GOHN, *Wien. klin. Wochenschrift*, 1901, p. 984; and ELSEY, *Jour. Medical Research*, 1905, N. S., Vol. VIII, p. 89.

(2) Vide, DUNHAM, *Proceedings of this Society*, 1905, N. S., Vol. V, p. 134.

gococci isolated from the spinal fluids or from spinal exudates at autopsy they had in every case obtained acid fermentation in dextrose and maltose serum water. Other micro-organisms from other sources, although morphologically like the meningococcus (including the gonococcus and catarrhalis cultures), failed to give such sugar reactions. Some of the strains fermented maltose and dextrose, but fermented other sugars also. The meningococcus produced a certain amount of fermentation after three to five days in dextrose and maltrose, but never coagulated them. In working with a few micro-organisms isolated from the knee joints these fermentations were absent in almost every case. In view of the fact that the meningococcus apparently always ferments these two sugars it would seem that this was a point where that micro-organism at any rate could be differentiated.

DR. E. LIBMAN said that in a paper read by Dr. Celler and himself before the Society in December 1902, it was stated that the meningococcus could produce a small amount of acid in glucose. Later they had found that it produced acid also in lactose but not in saccharose. Maltose had not been tested. To determine the presence of acid production with such an organism as the meningococcus one would have to make use of optimum media. Dr. Celler and he had determined the acid production by the presence of precipitation in media containing agar, serum, and the carbohydrate to be tried. When a medium 1.5 per cent. acid was used it required but little acid production to throw out a precipitate.

DR. WADSWORTH said that he had tried the growth of this organism in the inulin serum media of Hiss, but did not recall whether it was before or after the organisms had been adapted to artificial media. He had not got growth at that time.

FURTHER STUDIES ON SPIROCHETES.

L. B. GOLDHORN.

Mr. L. B. Goldhorn said that at the last meeting of the Society he had had the pleasure of presenting a rapid staining method for the *Spirochæte pallida*. During an extensive use of this method he had found some things which were new to him and which might be of interest to the members of the Society. In the first place he wished to draw attention to the fact that he had modified his staining method in so far as he now followed the stain with a wash in Gram's or Lugol's solution for ten or fifteen seconds. The spirochetes are then stained a bluish black and are very suitable for photomicrography.

Mr. Goldhorn showed a large number of photographs which illustrated the various steps which he would describe. So far he had had the opportunity of examining fifty-four undoubted cases of syphilis, and besides these a large amount of non-syphilitic material. He had not found *pallida* in any case except of undoubted syphilis. So far as the undoubted cases were concerned, eight of them had remained negative. Of these some were interesting. In the first place, the majority of chancres showed only *pallida* and no other organisms, but a great deal depended upon the technique. In curetting a chancre he invariably curetted at the edge and in this way obtained a small amount of serum and a very few red corpuscles, which showed little outside of these constituents and the *pallida*, the latter usually in rather large numbers. In some chancres, *refringens* had been found as well as *pallida*. One case of mixed lesion had remained negative. A case of primary lesion on the tongue and penis simultaneously also remained negative.

Another case was a two days chancre of eight days incubation which remained negative. Another of a four days chancre with three days incubation showed enormous numbers of refringens but no pallida. Of the secondary lesions, the most interesting case was that of a married woman who had a general papulo macular eruption. Two macules, one on the arm and one on the shoulder, were curetted and showed an enormous number of Spirochæte refringens and some other spirochetes after the thorough removal of the epithelial layer. This proved that the refringens occurred in other localities than on mucous membranes. It should be stated that the patient had some acne. On the other hand, in these two secondary lesions on the skin no pallida was found. The same woman had under the left breast a moist papule, and on making preparations from this papule enormous numbers of the pallida were found. No pallida was found anywhere but in this little papule under the left mamma. This was a very undisturbed spot, the breast perfectly protecting the papule. He had seen no other cases which showed the pallida in such enormous numbers. In another case of a man with a macular eruption and moist papules on the scrotum, the macules remained negative and the papules again showed the pallida though in this case but very few. Another case of a woman under treatment with mercurial injections was examined for six consecutive weeks, and on each occasion the pallida was found. Another woman with a mucous patch in the mouth was examined for three consecutive weeks. The first examination was positive, the second negative, and the third again positive.

Mr. Goldhorn had changed his technique of obtaining specimens, inasmuch as he now preferred to make impression preparations (*Klatschpräparate*) whenever

that was possible. By making these the pallida was obtained in a more or less undisturbed position. These preparations showed many new things. German observers had spoken a number of times of the pallida leaning upon red corpuscles while it seemed to shun the leucocytes. These preparations showed that pallida was just as often leaning against leucocytes as against red corpuscles.

In examining patients it is often necessary to make many examinations; in some cases which at first were negative pallida had been found on subsequent examinations. Again, Mr. Goldhorn thought it necessary when there were multiple lesions to examine several of these. One might find the pallida in one locality and not in another in the same patient.

As regards the morphology of the parasite, he had not infrequently seen in photographs one or two granules in the body of the *Spirochæte pallida* and had thought it possible that these granules might be a nucleus. As far as the flagella were concerned, studies of fresh material had never permitted him to see these. In stained preparations he had occasionally seen a terminal prolongation which looked like a flagellum. This flagellum was found but rarely even though the preparation was an impression preparation. One might look over hundreds of spirochetes before finding such a terminal prolongation. Among the photographs were some which showed what appeared to be one pallida attenuated in portions. Such an arrangement presented in his opinion several organisms end to end, the grouping following longitudinal division of which he intended to adduce proof. One could not imagine terminal flagella in this instance unless one regarded the series as a single organism with two terminal flagella, present but not stained. Not infre-

quently when a flagellum-like prolongation was found, it seemed to be rather too coarse to be a true flagellum. He did not think it likely that it was the fault of the stain because similar results were obtained by the Loeffler method which was supposed to stain the flagella. Therefore he did not feel justified in believing in the presence of a flagellum from his own researches.

The number of curves was found to vary greatly. One photograph shown had a pallida with twenty-nine; others had as few as five or six. The one with twenty-nine was undoubtedly a single individual as it was uninterrupted and of even diameter throughout. In other cases in which the organism showed a large number of curves and thinned out intermediate places, closer inspection led one to believe that one was dealing with several organisms. Schaudinn himself claims that the pallida is a more or less rigid spiral. Mr. Goldhorn's photomicrographs showed portions of the pallida where the organism was very little bent or perfectly straight. In one instance he had thought he saw the nucleus lying just in this portion. He believed therefore that the organism was very flexible although its appearance in a living state was spiral. As illustrating the various forms of the parasite several figures taken from photomicrographs were shown. Figure 'A' was a rather thick organism, attenuated at one end, which ended in three distinct individuals. It did not seem possible that this was an accidental overlying of several organisms. Figure 'B' showed something which might be taken for an accidental overlying. Under the microscope however there was a specimen which in one field of an oil-lens showed five individuals which were closely intertwined. Figure 'A' was thought to represent longitudinal division. In Figure 'C' the spirochetes were grouped around a refractive

granular body to which attention had already been drawn at the last meeting. These bodies were very numerous in some preparations. They were highly refractive, whitish, and did not take any stain except for the granules. Their proximity to the pallida and their relationship was very suggestive. They might be degeneration products, but Mr. Goldhorn did not know of any hyaline, or refractive degeneration products. He merely wished to draw attention to these bodies and to state that he could not account for them. Figure 'D' showed a sort of zooglea. It illustrated the grouping which had been described by him at the previous meeting, when it was stated that a number were lying together, the ends seemingly welded together.

As far as longitudinal division was concerned there seemed to be a rather constant repetition of the number of pallida formed. It seemed that the division did not result in the formation of two, but of four individuals. When the division was completed the four seemed to remain attached to each other and formed a more or less straight line. The intertwined ones were frequently longer than the ordinary pallida and for this reason a photograph was exhibited which showed four pallida of the ordinary size and appearance which were only one-half as long as these intertwined ones.

In conclusion, Mr. Goldhorn stated that he was of the opinion that this organism is not a bacterium but a protozoon, which multiplies by longitudinal division.

EPITHELIOMA OF THE ESOPHAGUS WITH PERFORATION INTO THE TRACHEA.

E. LIBMAN, M.D.

This case is of interest from a clinical as well as from a pathological standpoint. The patient was a man, 34 years of age, who had a history going back a number of months, of severe cough, loss of weight and difficulty in swallowing. It was found that on swallowing food a coughing spell resulted and the food was regurgitated with a large amount of muco-pus. Even the swallowing of water brought on a paroxysm. There were signs on the right side in the interscapular region of what appeared to be a bronchiectatic abscess. It was believed that there was present a communication between the esophagus and the air passages. The appearance of the man pointed to new growth and the chances were in favor of that as it is the most common cause of such communication. No tubercle bacilli were present in the sputum.

An X-ray plate was made and this showed, near the root of the right lung, a round dense shadow, which was thought to be a calcareous mass due to old tuberculosis. This made it appear very probable that we were dealing with a communication due to the rupture of a traction diverticulum.

At the post-mortem examination a very large epithelioma of the esophagus was found with a perforation into the trachea measuring 3x4 cm. There was a large abscess in the posterior mediastinum communicating with the tumor. Near the root of the lung a large calcareous cheesy mass was found.

In this case, although the fluoroscope picture itself was correct, it led us away from a correct diagnosis.

A CASE OF HYPERNEPHROMA INVOLVING THE INFERIOR VENA CAVA.

N. E. BRILL, M.D., AND E. LIBMAN, M.D.

The patient was a man, 60 years of age, who had been ill for eleven months suffering from dull pain in the right hypochondrium. After two months he had had to discontinue work. Five months before admission to the hospital he noticed a large swelling in the right hypochondrium. The pain never became very intense and was never colicky. It did not radiate to the shoulder, but did radiate towards the ilium. There had been diarrhea for a short time.

On admission to the hospital there was found a very large irregular tumor filling up the right hypochondrium and extending down to the right iliac fossa. It was difficult to decide whether this was a tumor of the right kidney or of the intestine, or whether the tumor was a lymphosarcoma springing from the retroperitoneal lymph nodes. The skin showed a peculiar lesion accompanied by pruritus, which more commonly occurs with lymphosarcoma (Dr. Lustgart). There was at no time any hematuria. Ureteral catheterization was performed by Dr. Berg. The catheters could be passed to their full length on both sides, but on the right side no urine could be obtained. It seemed more likely then that the growth started in the kidney, and such being the case, lymphosarcoma was considered less likely than hypernephroma.

Before the patient entered the hospital he had had for a short time edema of both feet; while he was in the hospital there was slight edema of the right foot.

The autopsy revealed this large tumor of the kidney which I now show you. The growth shows a striking yellow color except for the hemorrhagic areas. The en-

tire kidney was involved, except a small area at the upper pole. The pelvis was completely blocked. The growth had extended into the inferior vena cava as far up as the diaphragm, the lumen being almost entirely closed off. It also extended along the wall of the inferior vena cava as far as the iliac veins, and into the left renal vein. There were a number of small metastatic nodules in the liver and in the lungs; there were some larger nodules of a more whitish color. Over the right middle lobe on the pleura the metastases had taken the form of small polypoid growths. There was one small nodule in the wall of the left ventricle near the apex. The microscopic examination of all the growths showed a typical hypernephroma.

The absence of marked distention of the veins of the lower extremities and of marked edema, notwithstanding the decided obstruction in the inferior vena cava, was of interest; but the absence of local signs in this condition is not as uncommon as is generally supposed.

THE PHOTODYNAMIC ACTION OF EOSIN AND ERYTHROSIN UPON SNAKE VENOM.

HIDEYO NOGUCHI, M.D.

This paper deals with the effects of two active photodynamic chemicals, eosin and erythrosin—chosen on account of their pronounced action with ferments and toxins—upon the toxic principles of venom. Snake venom is of a complex nature, with its independent toxic principles—neurotoxins, hemolysins, hemagglutinins, cytotoxins, hemorrhagin, thrombokinase, and precipitin.

They vary greatly in lability; hemorrhagin, the predominant poison of rattlesnake venom, is destroyed at 75°, as is thrombokinase, which is largely contained in daboia venom; while at that temperature neurotoxin, the chief principle of cobra venom, suffers little change.

The venoms of the cobra, *Crotalus adamanteus*, and *Daboia Russellii* were exposed to the action of eosin and erythrosin in sunlight and in the dark.

In cobra venom tested against the blood of dogs, the hemolysin is reduced very little in activity by exposure to sunlight in the presence of eosin, and not at all in the absence of that dye or in the presence of erythrosin, showing the stability of the compound and the resistance of the hemolysin, to the photodynamic action of these two fluorescent bodies. The results differed from *Crotalus* venom; its hemolytic power being reduced by almost 200 times its original strength when measured by absence of hemolysis, and almost forty times when measured by slight hemolysis. The dyes are without influence in the dark, and direct sunlight does not injure the hemolysin in the colorless solutions. Cobra and *Crotalus* hemolysins exhibit, therefore, wide differences in susceptibility to injury by these dyes, daboia venom occupies an intermediate position, its loss of power when acted upon by eosin or erythrosin in the light varies between $\frac{1}{2}$ and $\frac{1}{4}$ %. Eosin with both rattlesnake and daboia venom appears to be slightly more active than erythrosin. These tests showed that hemorrhagin, the predominant principle of *Crotalus* venom, is only slightly resistant; that coagulin of daboia venom is more resistant; and that neurotoxin, as represented in cobra venom, is very resistant to photodynamic action.

The two anilines have no marked effect in diminishing the toxic activity of cobra venom for guinea-pigs.

On the other hand, for rabbits a reduction in toxicity of about $\frac{1}{3}$ is apparent after the eosin treatment.

In testing guinea-pigs with *Crotalus* venom the action of the dyes, after exposure to sunlight, takes place chiefly upon the hemorrhagic principle, and to a less degree upon the neurotoxic principle of the venom. The action of eosin in light upon *Crotalus* venom is rapid, in eight hours about 9.6 minimal lethal doses and about 16 minimal hemorrhagic doses were completely destroyed; while thirty hours is an insufficient length of time to reduce markedly the toxicity of cobra venom.

A series of experiments upon rabbits with daboia venom exposed to the action of the fluorescent dyes in sunlight shows that the toxicity is considerably reduced, and the thrombokinase completely destroyed: seventy-five minimal lethal doses of eosinised venom may not contain one minimal lethal dose of the bloodclotting principle.

The globulin precipitating and red corpuscle protecting principle of cobra venom, previously described by me, does not undergo marked change after an exposure of twelve hours to sunlight in the presence of the anilines. If erythrosin, in a strength of one per cent. of the mixture, is present, the venom-hemaglobin precipitation does not occur, and the corpuscles are prevented from protection against hemolysis. In respect to this action of erythrosin, Sacharoff and Sachs state that in solutions of high concentration this dye is itself hemolytic.

In concluding it may be said that venom-neurotoxins are highly resistant to photodynamic action, venom-hemolysins are less resistant, while the hemorrhagin and thrombokinase of *Crotalus* and daboia venoms exhibit weak powers of resistance to the action of anilines. Hence it follows that while cobra venom remains almost

unaltered, rattlesnake and daboia venoms are greatly reduced in toxicity when mixed with fluorescent dyes and exposed to the sunlight. In stability of hemolysin, cobra venom ranks first, daboia second, and *Crotalus* third. Thus the chemical complexity of the chemical constituents of the venoms has again been shown.

The globulin-precipitating and blood-corpuscle-protecting principle of cobra venom is relatively thermostable, and, in contradistinction to the immunity precipitins, it is also unaffected by eosin and erythrosin.

There is an interesting parallel between the action of eosin and erythrosin upon the different venoms and their reactions to other injurious agencies. For example, the hemolysins of cobra and daboia venoms are more heat resistant than the hemolysin of *Crotalus* venom, and the former are less injured by the dyes than the latter. The neurotoxin of the former venoms is also more thermostable than that of the rattlesnake, and the same relative degree of resistance holds for this substance and the anilines. Just as the hemorrhagin of rattlesnake venom and the thrombokinase of daboia venom are destroyed by a temperature of 75° C., so are they readily inactivated by the photodynamic substances employed; thus proving that this form of destructive activity is affected by the same conditions of resistance as confront the action of the usual chemical and physical agents.

THE EFFECT OF EOSIN UPON TETANUS TOXIN AND UPON TETANUS IN RATS AND GUINEA-PIGS.

SIMON FLEXNER, M.D., AND HIDEYO NOGUCHI, M.D.

Jodlbauer and v. Tappeiner studied the action of certain fluorescent substances upon diphtheria and tetanus toxins. They found that when the toxins were mixed with 0.05 per cent. of eosin and exposed for three days to diffuse sunlight their toxicity was greatly diminished. The sample of tetanus toxin so treated produced, in 1 to 10 minimal lethal doses, local tetanus only, while in 25 minimal lethal doses and over it was fatal. Huber stated that the addition of one per cent. of eosin to tetanus toxin, and an exposure of six hours to the sunlight, suffice to destroy the poison, but if the mixture is kept in the dark the poison is not deprived of its toxicity. The dose used by Huber in testing toxicity was one minimal lethal dose. Huber also noted a loss of hemolytic power.

Our experiments were begun last spring and were completed before Huber's paper appeared. They embrace the study, first, of the influence of certain aniline dyes upon tetanolysin; second, the effect of eosin upon tetanospasmin; and, third, the influence of eosin upon the course of experimental tetanus in rats and guinea-pigs.

Our experiments on tetanolysin were made with two samples of the toxin: one a dried ammonium sulphate precipitate of bouillon cultures, and the other a fresh filtrate of bouillon cultures. The first was used as a four per cent. solution; the second in full strength, sterile salt being added to produce isotonicity. The determination of initial hematoxicity showed complete hemolysis with

0.1 cubic centimeter of the first sample, and with 0.7 cubic centimeter of the second.

Two cubic centimeters of tetanolysin (representing about 150 minimal hemolytic doses) are completely destroyed by 0.3 cubic centimeter of a one per cent. solution of eosin, in one hour in the dark, at 37° C. In other words, an eosin strength of 0.13 per cent. quickly destroyed the lysin.

Simple exposure of tetanus toxin in test-tubes for six hours completely destroyed the lysin; and an exposure for two hours in the presence of 0.03 c.c. eosin solution to 2 c.c. of the toxin also destroyed the hemolysin. In the dark this small quantity of eosin has no effect upon the lysin. The action of eosin in the light is very rapid, since after ten minutes' exposure the hemolytic property may be lost.

A series of experiments was made with Grüber's methylene blue, orange G, fuchsin, orcein, and vesuvin. Berlin blue was also tried. The results may be summarized as follows: In strengths of 0.2 per cent. and above, methylene blue and vesuvin destroy tetanus hemolysin in one hour. Quantities below 0.1 per cent. are partially destructive only; while 0.04 per cent. no longer checks hemolysis. Fuchsin, orcein, and fluorescein are also injurious, but their limits of action were not determined. Berlin blue is without effect.

These experiments bring out the fact that aniline dyes, fluorescent ones chiefly, have an effect upon the labile hemolysin in the dark, although the effect is less than in the light.

The fatal constituent of tetanus toxin is the convulsive agent tetanospasmin, which has an especial affinity for nervous tissues. We tested the action of eosin in the dark as well as in the light upon the convulsive prin-

ciple. As regards the latter we confirmed the results obtained by previous experimenters. To one cubic centimeter of the toxin were added varying amounts of five per cent. eosin. The mixtures were kept one hour at 37° C. before injection into the right gluteal region of white rats, weighing about ninety grams each. The animals were kept in a room diffusely lighted; the cage was partly shaded. The toxin employed was fatal in four days in a dose of 0.0025 c.c., the first symptoms of tetanus appearing in twenty-four hours; 0.0005 c.c. was the minimal tetanic dose, and 0.001 caused strong tetanus but was not fatal. Doses of about 0.4 c.c. caused death in from 24 to 48 hours. Hence one cubic centimeter of the toxin contained about 400 minimal lethal doses and 2000 minimal tetanic doses for the rats.

It was shown that eosin in solutions exceeding one per cent. in strength quickly destroys tetanospasmin in the dark, and in 0.6 per cent. solutions greatly reduced the activity of the poison. The chronic nature of the tetanus which the modified poison produces is a striking and interesting occurrence.

In a series of experiments in which the toxin and eosin were injected simultaneously, but separately, into rats, it was found that the effect of the eosin upon the course of the tetanus consisted in delaying the onset of symptoms and in prolonging the period of intoxication. Since the toxin employed caused, in control animals, in doses of 0.0025 c.c., tetanic symptoms to appear in twenty-four hours, the delay of symptoms in the eosin-treated animals is at once apparent; while the prolongation of life is also brought out by the experiments. However, none of the animals of this series was actually saved. And in view of this fact the question arises whether, after all, eosin exerts a destructive action *in vivo*.

at all comparable with its effect *in vitro*. Since, in all but one rat, the eosin injection was made about that of the toxin, and since eosin alone in five per cent. solution causes edema of the tissues, perhaps changes in the absorption may account for the delay of onset of the symptoms and fatal effect. But this explanation does not entirely account for the effect observed, as in Rat 5 the injection of the poison in one side and the eosin in the other side of the body was made, and yet the fatal result was delayed.

It is recognized that poisoning with tetanus toxin is not an exact equivalent of infection with tetanus bacilli, for while in the first the full fatal dose of poison is at once available for fixation by the tissues, in the second the appearance of the first symptoms of tetanus may not exactly coincide with the presence of a fatal quantity of the poison in the body. If, therefore, eosin is capable of modifying tetanus poison in such a manner as to diminish its toxicity when kept in contact for a short time at body temperature, even in diffuse light and in the dark, the important question arises whether this action may be exerted in the body to an extent sufficient to rescue infected animals. To imitate natural conditions more closely, silk threads carrying tetanus spores but no toxin were introduced beneath the skin of the right thigh. Some of the animals remained untreated; others were treated with eosin in various ways. This series of experiments indicated that the power of eosin to destroy or modify the tetanic poison in the body, while marked, is not absolute. However the eosin is brought into the body of the infected animals, it causes an increase in the period of intoxication and delay in the supervention of death. If the eosin solution is sufficiently concentrated and is brought into relation with the focus of develop-

ment of the tetanus spores, it is capable not only of modifying the tetanus but of wholly suppressing its development.

A parallel series of experiments to the latter, carried out on the more highly sensitive guinea-pig, showed that even in the guinea-pig tetanic symptoms may be restrained, provided the eosin is brought into close relationship with the developing tetanus poison before it is fixed by the nervous tissues or reaches the general circulation.

Discussion.

DR. C. W. FIELD asked whether in the course of these experiments the fatal dose of eosin for guinea-pigs and rats had been determined.

DR. NOGUCHI said that he had used a five per cent. solution, injecting 1 c.c. under the skin. On exposure to the sunlight the animals died within two hours. The eosin had never killed the animals when they were left in the dark. He had used 0.2 to 0.5 c.c. of a five per cent. solution of eosin, giving it every twenty-four hours, but had never injected more than 1 c.c. because of its tendency to cause extensive necroses.

A CASE OF SYPHILIS OF THE STOMACH.

A. M. PAPPENHEIMER, M.D.

Dr. A. M. Pappenheimer reported briefly on a case of syphilis of the stomach. The patient was a man 32 years of age, a cook. He had been ill for four or five months previously, with vague symptoms pointing to a chronic ulcer. There had been no vomiting until a day

previous to his admission to Bellevue Hospital, when, without apparent cause, he had a sudden severe hemorrhage. On autopsy, interesting lesions were found in the stomach and liver.

The stomach was rather small. It contained a recent red blood clot, about the size of an orange. The mucous membrane on the posterior wall near the lesser curvature, was the seat of an extensive serpigenous ulcer, involving an irregular area approximately 6x5 cm. The ulcer had the following characteristics: The edges were irregularly sinuous, slightly raised, not indurated. The floor of the ulcer was formed by the submucosa. It was clean, and not covered by slough. There were a few islands of intact mucosa within the confines of the ulcer. About 2 cm. from the left border of the cardiac orifice, just within the margin of the ulcer, were seen the eroded stumps of two vessels, which projected several mm. above the mucosa. About 3 cm. from the pyloric ring, along the greater curvature, was a small polypoid outgrowth and adjacent to this, a superficial irregular ulcer, about 2 cm. in diameter, having the general characteristics of the larger one just described. In the floor of this second ulcer, was a small whitish nodule. Near the greater curvature, about 10 cm. from the pylorus, was a small superficial erosion of the mucosa.

The wall of the stomach from the pyloric ring to beyond the limit of the ulcer, showed marked thickening. This was due to the replacement of the submucosa by firm, whitish, infiltrating tissue, which on cross section was about 5 mm. in thickness. The muscular layer was about 2 mm. The mucous membrane not involved by the ulcers was everywhere somewhat swollen, in places mammillated, and covered with tenaceous mucus. The peritoneal surface of the stomach was normal.

The liver showed typical tertiary syphilitic lesions, with numerous deeply constricting bands of cicatricial tissue, and multiple gummatous nodules.

The pancreatic, perigastric and mesenteric lymph nodes were all enlarged, ranging from 1 to 3 cm. in diameter. Section through these lymph nodes showed circular areas of firm whitish tissue, between which were recent reddish hemorrhagic extravasations.

Discussion.

DR. E. LIBMAN said that they had seen very little of this condition at Mount Sinai Hospital. A case observed last summer was of great interest. Resection of the pylorus was done for supposed carcinoma, but the inspection of the gross specimen suggested the diagnosis of syphilis by exclusion. There were irregular ulcerations just as in Dr. Pappenheimer's case and there were scars at the base of the ulcers. The patient died two days after operation, and a typical syphilitic liver (hepar lobatum) was found. The microscopic examination was in accordance with the diagnosis.

A CASE OF CONGENITAL HEART DISEASE.

E. P. BERNSTEIN, M.D.

DR. E. P. Bernstein presented a case of congenital heart disease. The remarkable nature of the specimen warranted a résumé of the clinical history. The family history was negative, the parents having had three children, two of whom were perfectly well. This child was born at full term. The question of asphyxiation at birth

was doubtful. Up to his sixteenth month he was apparently well, both in appearance and action. His first tooth appeared at the sixth month, and he began to walk at one year. When he was sixteen months old, he developed a cough and for that reason a physician was consulted, who told the mother that the child had heart trouble. During the summer of 1905, the child was taken to Mount Sinai Dispensary because his condition had become suddenly worse. He ceased to walk, he coughed a great deal, his breathing was labored, and he had lost his appetite. At this time, the physical examination showed marked cyanosis of all the mucous membranes and skin. His fingers and toes were decidedly clubbed. His eyes were prominent. He showed a geographic tongue. His lungs gave signs of a bronchitis. His heart showed the following: Apex beat in the 5th intercostal space in the mammary line, giving a fairly strong, diffuse impulse. The upper border was in the 2d intercostal space; the right border, slightly to the right of the right edge of the sternum. The left border was in the anterior axillary line. Over the entire precordium was heard a loud systolic murmur, most marked in the 2d left intercostal space. The pulses were equal, regular, and fairly full, being 120 to the minute. The liver was somewhat enlarged to percussion, its free border being easily palpable. The spleen was also slightly enlarged. A count of his erythrocytes showed them to be 10,600,000 to the c.mm. The child's condition gradually improved without any special treatment except hygiene and diet, until he contracted an attack of influenza and suddenly became much worse. Dr. Bernstein was called, and found him in coma, his face pale (this being in marked contrast to his usual cyanosis), the apex beat weak, the pulse small and arrhythmic. His respirations were rapid and

with great muscular effort. Temperature, 101°. He remained comatose for four hours, but had similar attacks for ten days before death, at which time he was two years eight months old.

The diagnosis of congenital cardiac disease was evident, but the exact type was not determined. Unfortunately, permission for autopsy was limited to a small abdominal incision, and the examination was consequently incomplete. The heart was the only organ removed.

From an anatomical standpoint it showed the type of a true mammalian heart, having two auricles and two ventricles; but functionally it was almost a typical reptilian heart, the right auricle being but an atrium for the left auricle, the auricular septum being entirely absent except for a small strand. No blood could enter the ventricles from this atrium except through the left auricle. The right ventricle was but a mere slit in the wall of the left ventricle, having absolutely no function – the conus arteriosus dilating and forming a so-called third ventricle. At the origin of the aorta, under the right aortic flap, was an opening the size of a quill leading from the left ventricle into the conus arteriosus. Through this small opening all blood to be aerated must pass, and the presence in this opening of a vegetative polypoid mass, tightly adhering to its edge and almost entirely closing it, probably was the direct cause of the terminal convulsions and death. It probably acted as a ball valve thrombus, closing off the circulation. The left ventricle was dilated and the walls considerably hypertrophied. The mitral, aortic, and pulmonary valves were not diseased. There being no right ventricle present, the tricuspid valve was also absent. The aorta showed an anomaly, inasmuch as it had four main branches coming from its arch. Whether there were any bronchial, esopha-

geal, or pericardial arteries which may have supplied blood to the lungs could not be determined because of the limited autopsy permitted. The ductus Botalli was closed. The blood current must have been as follows: from the venous system, through the superior and inferior venae cavae, to the right auricle, from there to the left auricle, then into the left ventricle, where it was divided into two channels, the smaller through the opening under the right aortic flap into the conus arteriosus, pulmonary artery and lungs; the larger through the aorta, to its branches.

The case could be put down as a congenital cardiac disease with a polypoid thrombus, two very rare conditions. The remarkable points of this case were that the disease was not suspected until the child was sixteen months old, and then only because the child was treated for bronchitis, and that the child lived to be two years and eight months old with such a heart.

A CASE OF ADENOMYOMA OF THE UTERUS.

D. S. D. JESSUP, M.D.

The specimen which I have to show was removed from a woman, thirty-six years old, unmarried. Her general health had always been good. Two years ago she noticed a lump in the right of the abdomen low down. This continued to grow in size but caused no pain or discomfort until three weeks before operation. At operation the tumor was removed with the uterus and adnexæ. The patient left the hospital nineteen days later, being discharged cured.

Gross examination showed an enlarged nodular

uterus, 14x12x10 cm., which on section contained several fibroid nodules. The ovaries were fibro-cystic. The tumor, which appeared to be a subperitoneal fibroid, was 12x11x8 cm. It was nodular and very hard, and on section showed the structure of a fibromyoma. Near one border was a cavity, 1.5 cm. in diameter, filled with dark brown fluid, and near it and scattered through other portions of the mass were smaller cavities. Several of these were just beneath the peritoneum.

Microscopical examination of the cysts in the detached fibroid showed cavities lined with stratified cylindrical epithelium. There were also narrow channels and single glands scattered through the fibromyomatous tissue which were lined with similar epithelium. In certain places ciliæ could be demonstrated on the epithelial cells.

Sections of the fibroids in the uterine mass showed ordinary fibromyoma.

Cullen in his monograph on Adenomyomata of the Uterus, has divided them into three general classes, diffuse adenomyoma, submucous, and subperitoneal. This tumor seemed to conform with the description of the tumors which he places in the third subperitoneal class. The origin of these glandular elements is generally believed to be remnants of the Wolffian bodies.

INTRACELLULAR DIGESTION BY PHAGOCYTTIC CELLS.

E. L. OPIE, M.D.

It is well known that two types of cells are especially concerned in phagocytosis; these are the polynuclear leucocytes, which show a special tendency to take up micro-organisms, and certain large mononuclear cells,

which are concerned in phagocytosis of a variety of cellular elements. These cells are of the large mononuclear type corresponding to similar cells found in the blood. If red blood corpuscles are injected into the peritoneal cavity of guinea-pigs it is known that it is particularly these cells which take them up. These cells are also concerned in the phagocytosis of a variety of micro-organisms, particularly malarial parasites and trypanosomes. Metchnikoff makes a distinction between microphages, which take up bacteria, and macrophages, which take up red blood corpuscles and other cellular elements derived from the animal kingdom. Metchnikoff believes that the complement, or as he says, the cytase, which is concerned in the destruction of bacteria is derived from the microphages, and he speaks of it as microcytase; while the complement which is concerned in destroying red blood corpuscles is derived from the macrophage, and he calls this macrocytase. I do not intend to discuss the relation of the complement to the leucocyte; indeed, the origin of complement is still much disputed. Metchnikoff maintains that the complement is analogous to the proteolytic ferment of the phagocytic cell and the same view has been held by Buchner. It is this proteolytic ferment that I wish to discuss.

Examination of microscopic objects has proved that the undigested material disappears within the substance of the phagocyte and various attempts have been made to isolate from the leucocyte a ferment capable of destroying proteids. It has long been known that leucocytes contain ferments which are capable of softening gelatin and dissolving fibrin. I have studied this digestion, by means of the Kjeldahl method determining the amount of nitrogen of coagulable proteid converted by digestion into an uncoagulable form, and have found

that if leucocytes are freed from serum, a ferment capable of digesting both in an alkaline and in an acid medium is obtained. That is, the leucocytes act like pepsin digesting in acid media, and like trypsin digesting proteid in alkaline media. The purpose of my experiments has been to determine whether one ferment was concerned which dissolves proteid in the presence of alkali, in a neutral medium, and in the presence of acid, or whether there were two ferments present, analogous to the ferments in the digestive tract.

Cells were obtained by centrifugalization of an exudate, which was most readily produced by injecting aleuronat into the pleural cavity of a dog. The exudate thus obtained was very rich in cells. The cells were carefully separated from the serum by washing in salt solution, and were then accurately measured and suitably diluted with salt solution. A measured quantity of this suspension was allowed to act upon a measured quantity of proteid, for example, heated blood serum, for a number of days at body temperature; the amount of proteolysis was tested in an acid medium, the best being two-tenths per cent. acetic acid, in a medium with unchanged reaction, and in an alkaline medium, two-tenths per cent. sodium carbonate.

An attempt was made to preserve the ferments of leucocytes indefinitely. A glycerin extract preserves the enzymotic action for a long time, and is active in the presence of both acid and alkali. A dried powder from these cells preserves the power of the cells to digest in an alkaline or neutral medium, but by this means the power to digest in an acid medium is lost. Thus it might be supposed that there are two ferments present, and the effect of heat gives further evidence that two ferments are concerned. If the cells are heated to 70° C.,

both ferments are destroyed, but at 65° or 55° C., that ferment which digests in acid media is alone injured, while the ferment digesting alkali is practically unharmed. From these experiments the conclusion has been reached that two ferments are present in the leucocytes of an inflammatory exudate.

Since with the progress of inflammation, the cellular constituents of an exudate change, an attempt was made to determine if any relation existed between one or the other of the ferments and the particular types of exuded cells. When aleuronat is injected into the pleural cavity polynuclear leucocytes migrate from the blood vessels and at the end of from fifteen to twenty-four hours the exudate contains almost wholly polynuclear leucocytes with a certain proportion of mononuclear cells which do not exceed ten or fifteen per cent. The number of mononuclear cells gradually increases and at the end of from three to five days is from thirty to thirty-five per cent. The change which occurs is not well represented by these figures for the mononuclear cells have increased enormously in size and are actively phagocytic. They take up red blood corpuscles and often contain six or more polynuclear leucocytes.

It was found on comparing an exudate one day old with, for example, an exudate five days old, that the power of the cells to digest in an alkaline medium remained practically unchanged or had undergone slight diminution, while the power to digest in an acid medium had undergone a decided increase. In one instance the mononuclear cells at the end of twenty-four hours were fourteen per cent; at the end of five days, twenty-seven per cent. The power of the fresh cells to digest in acid media represented in terms of $n/10$ sulphuric acid at the end of twenty-four hours was 10.05 c.c.; at the end of five

days this power had increased to 18. c.c. It must be borne in mind that the rapidity of action with such a ferment is not proportional to the amount of ferment but is roughly proportional to the square root of the amount of ferment, so that the significance of this difference is greater than appears at first sight. In another instance the mononuclear cells were increased from twelve per cent. to twenty-three per cent., and the power to digest from 6.5 to 12.9 c.c. A number of other experiments with the same results might be cited.

It was observed that the lymph glands below the sternum increased in size as the pleurisy induced by the aleuronat progressed. Microscopical examination of these glands showed that the sinuses contained an enormous number of very large phagocytic cells, so-called macrophages, identical with those of the exudate. The substernal glands for this reason afforded a convenient opportunity to study the fermentative action of these cells. A suspension was made by forcing the gland tissue through a fine sieve, then measuring the cells in a centrifuge tube and diluting them to a proper amount with salt solution, so that comparisons might be made. These cells digested only in an acid medium and failed to digest in an alkaline or neutral medium. Normal substernal glands are so small that a sufficient quantity of cells could not be obtained for a comparative test, and to compare the substernal glands with relatively normal glands it was necessary to use mesenteric glands which contain only a moderate number of large mononuclear cells. Cells from the substernal glands at the end of from three to five days after the injection of aleuronat show a greater ability to digest proteid in an acid medium than those of the relatively normal mesenteric gland; that is, while a normal gland has the power of di-

gesting in an acid medium, with inflammation its activity is very much increased. In these experiments the increase was in the following proportions: 11.4 to 9; 11.5 to 8.75; 12.2 to 9. Here too the relatively slight though constant difference is of more significance than at first sight appears. When substernal glands at various intervals after injection of aleuronat were used, it was found that there was a gradual increase from 7.6 c.c. at the end of twenty-four hours, to 12.2 c.c. after five days, these figures representing the power of the glands to digest proteid.

Conclusions from the experiments described are as follows:

The cells of an inflammatory exudate are able to digest proteids both in acid and in alkaline media. By preparing a dried powder from such cells the power to digest in an acid medium is destroyed, and the power to digest in alkaline or neutral media is retained, thus indicating that two ferments are present. The two separate ferments are affected differently by different temperatures. As an exudate increases in age the mononuclear cells increase in number and at the same time the power to digest in acid media increases. The neighboring lymphatic glands with the progress of the inflammation contain an increasing number of mononuclear phagocytes and in accordance with this change there is a gradual increase of the power of these glands to digest in an acid medium.

Discussion.

DR. SIMON FLENNER asked Dr. Opie if he had made any observations regarding the manner in which red corpuscles were disposed of in the body; whether any particular set of cells was concerned in the digestion of red

blood cells; and what the composition of an exudate was in this case.

DR. OPIE said that in some experiments which he had not mentioned red blood corpuscles of the rabbit, carefully washed, were injected into the pleural cavity of the dog. This exudate differed from the exudate produced by aleuronat in that at the end of twenty-four hours the proportion of mononuclear cells was about thirty per cent., while the proportion with aleuronat was about ten per cent., and the power of the cells of the exudate produced by the red blood corpuscles to digest in an acid medium was considerably greater than that of the cells of the exudate produced by aleuronat.

ISOLATION OF GRAM NEGATIVE DIPLOCOCCI IN THREE CASES OF ARTHRITIS, ACCOMPANYING URETHRITIS; IN A FOURTH CASE, WITHOUT URETHRITIS.

THOMAS FLOURNOY, M.D.

The following cases have been observed in Bellevue Hospital, during the past year, and the results of the bacteriological examinations have been considered unusual enough to warrant their being reported.

Dr. S. Alexander. Dr. Chetwood and Dr. H. M. Biggs, have kindly placed the clinical data at our disposal.

CASE I.

A. M., printer, 23 years of age, was admitted to the hospital in the service of Dr. Alexander, on December 22, 1905, three weeks after the onset of urethritis, with

purulent discharge, ardor urinae and frequency of micturition. On the day before admission, patient noticed pain in right knee, followed during the night, by swelling of the joint. No history of trauma was obtained.

At the time of admission, patient complained of pain upon sudden movement of the knee, and of tenderness on both sides at the line of articulation. Examination showed restriction of voluntary movement, normal range of passive motion, and no swelling of the joint. Overlying skin normal. Moderate amount of yellowish discharge from urethra.

Patient appeared to improve slightly under treatment; but on the fourth day after admission, temperature rose, and knee became more painful, and during the succeeding ten days, became red and swollen, with much effusion in and about the joint. Thirty-four days after the first symptoms of arthritis, a small amount of turbid yellow fluid was withdrawn by aspiration, and sent to the laboratory. At this time the urethral discharge had practically disappeared.

Microscopic examination of the joint fluid showed numerous pus cells and a few groups of intracellular Gram-decolorizing diplococci; also numerous faintly staining Gram negative bacilli. Ascitic-agar plates streaked with floccules from the fluid showed, after 24 hours, eight or ten colonies of diplococci, decolorizing by Gram method of staining. Beside these, the plates contained a few micro-organisms of varying morphology and staining reaction, which, with one exception, were believed to be merely contaminations. Only one colony was found which was made up of bacilli resembling those found in stained preparations from the joint fluid, and this growth was unfortunately not further investigated.

The colonies of diplococci were small, grayish, viscid

and translucent, and under the lens gave the appearance which is considered typical of colonies of gonococcus; that is, they were gray, with a slightly brownish tint, had fairly even circular border, and a moderately dense, coarsely granular, central portion, with lighter, finely granular peripheral zone. In the third and subsequent generations, transplants were made to glycerin-agar, and to ascitic-agar, in the following manner: The entire colony was picked up on a broad platinum streaker and spread over the surface of the glycerin-agar plate, and then, without reinoculating, over the ascitic-agar. On the glycerin-agar, a moderate, rather retarded growth was obtained in the fourth generation, and from these plates, three further generations were obtained, showing somewhat more abundant growth on the same medium. In view of the number of generations and the increased amount of growth with subsequent transplantations, we can exclude the possibility of our having transferred from the serum-medium, with the micro-organisms, enough of that medium to insure continuation of growth.

On January 18, forty-seven days after the onset of the arthritis, a second aspiration was performed, and 15 c.c. of turbid yellow fluid withdrawn. Stained films from this specimen showed pus cells and intracellular Gram-decolorizing diplococci, without other bacteria. Cultures on ascitic-agar yielded, in this instance, about thirty colonies of Gram-decolorizing diplococci, without other micro-organisms.

From the original plates, (first generation) seven colonies were streaked upon glycerin-agar and then upon ascitic-agar plates. All of these transplants yielded a fair growth and from the glycerin-agar plates, third and fourth generations were easily obtained upon the same medium.

The cultures from the two separate aspirations from this case were then transplanted upon Loeffler's blood-serum, gelatin and broth. Blood-serum tubes showed, after 24 hours, good growth in the form of small, raised, moist, grayish-white colonies, and inoculations from these to the same medium yielded always good growth. Broth tubes showed after two to three days, uniform cloudiness with coarse, somewhat granular deposit. Transplants, made after four or five days, showed the organisms to be still living. No growth was obtained in gelatin.

CASE II.

A. T., machinist, 27 years of age, admitted to Dr. Chetwood's wards on January 1, 1906. Had contracted a urethritis two weeks before admission. Gave history of a previous attack of rheumatism, lasting for one week, part affected not stated. Denied previous attacks of venereal disease of any kind.

Three days before entering hospital, patient injured his left knee in a fall, but continued working during the next day and a half, the joint meantime being painful, and beginning to swell. Two days after the injury, pain became severe and swelling interfered with movement of the leg. Physical examination showed swelling, redness and calor of left knee joint, with restriction of both active and passive movement. Inguinal lymph nodes enlarged and hard. Temperature 102°. Fourteen days after onset of arthritic symptoms, a small amount of flocculent fluid was withdrawn from the joint by aspiration. Microscopic examination showed presence of pus cells and of numerous intra- and extra-cellular Gram-decolorizing diplococci. Cultures upon ascitic-agar plates gave pure growth of diplococci, similar to those found in stained preparations. The colonies on these plates were in all

respects like those described and depicted for gonococcus.

Following the method previously described, transplants were made to glycerin- and to ascitic-agar. Although each generation after the first was tried in this way, no growth was obtained on glycerin-agar, during the first seven generations. Inoculations upon Loeffler's blood-serum, however, gave good growth, when first tried (eighth generation), and sub-cultures from these tubes gave good growth upon the same medium.

Transplantation to ordinary nutrient bouillon resulted in slight clouding of the medium and moderate flocculent deposit, but further bouillon tubes inoculated with these remained sterile. No growth was obtained in gelatin.

CASE III.

L. G., colored woman, 17 years of age, married, admitted February 19, 1906, to Dr. Chetwood's service, three days after bearing a healthy male child. About ten days before coming to hospital, patient had what she described as a boil on one of the labia, unaccompanied, she said, by vaginal discharge. About three days later, her right knee became swollen, hot and painful. Physical examination showed glands of Bartholin to be swollen and apparently tender, with small floccules of pus at the openings of the ducts. Inguinal lymph nodes large and tender.

Nine days after onset of symptoms of joint involvement, 12 c.c. of turbid yellow fluid were withdrawn by aspiration. Smears showed presence of large numbers of pus cells, but no micro-organisms were found. Streak plates of ascitic-agar, however, yielded pure culture of a Gram-decolorizing diplococcus, morphologically like go-

nococcus. Cultures from floccules of pus in vaginal discharge yielded considerable number of colonies of Gram-decolorizing diplococci.

Most unfortunately, all cultures from this case were lost before observations of their behavior upon other than serum-media could be made, and their identity remains, therefore, unknown.

CASE IV.

H. P., male, age 31, admitted April 18, 1905, to the wards of the 3rd medical division, service of Dr. Hermann M. Biggs. This patient denied having had venereal disease, though he admitted great sexual and alcoholic excesses during the week previous to onset of illness. Symptoms began April 10, with malaise, dizziness, weakness and gradually increasing pains in both legs, these pains finally becoming most marked in the right knee.

Physical Examination: Well developed and well nourished male. Skin hot and dry; marked general pallor; mucous membranes pale. Visible pulsation in vessels of neck. Lymph nodes palpable. Skin over right leg smooth and shiny; marked tenderness along popliteal nerve, and at the head of the tibia. Right leg cannot be voluntarily extended. Heart sounds of fair force. Faint blowing systolic murmur at apex; not transmitted. Faint systolic murmur at base, heard loudest in vessels of neck. Pulse rapid, regular, fair force and volume. Area of splenic dullness large. Organ palpable on deep inspiration.

Five days after admission, the following note was made: Right knee swollen, hot, tender and painful. Evidence of fluid in the joint. Right ankle also tender and painful. Hip swollen and tender. Cardiac mur-

murs are more distinct. Temperature 102°. Pulse 132. Respiration 28.

Fifteen days after onset of joint symptoms, blood cultures were made, and knee joint fluid withdrawn for examination.

At this time, examination of the urethral secretion, as well as of the urine, by both microscopic and cultural methods, failed to give any evidence of gonorrhoea.

Microscopic examination of the turbid joint effusion showed large numbers of pus cells and a few groups of flattened, Gram-decolorizing diplococci, within the pus cells. Ascitic-agar streak plates inoculated with the fluid gave pure culture of diplococci similar in morphology to those seen in the smears, decolorizing with Gram's method of staining.

In our hands, attempts to grow these diplococci upon other than serum media were unsuccessful during ten or more generations. Transplants given to Dr. Elser, however, have finally yielded a growth upon ordinary nutrient bouillon.

The plates made from the patient's blood, a mixture of blood and agar in a proportion of about one to five (1:5), showed, after forty-eight hours, a few, minute, deep colonies, examination of which showed them to be made up of diplococci morphologically identical with, and staining like those isolated from the joint fluid. Subcultures from these, were, however, unsuccessful, so that no identification could be made.

* * *

General considerations based upon the study of the micrococci isolated from these few cases bring out some interesting facts. In the first place, because of their cultural characteristics, none of these strains can be held to be gonococci, since they have all been grown upon

culture media believed to be unsuitable for the growth of the true gonococcus.* Moreover, these cultures vary in themselves, in a manner to be described below.

We have, therefore, micro-organisms from cases which are clinically gonorrhoeal arthritis, and yet these micro-organisms are not gonococci, and moreover, are not of the same species. The examination of stained preparations made directly from the fluid aspirated in any of these cases would perhaps ordinarily have been taken to be sufficient to establish a diagnosis of joint infection with gonococcus. Cultural methods, however, show that the diplococci seen in smears are not gonococci.

From each of these cases, then, there were isolated from the affected joints diplococci which, in morphology and staining reactions, bore a close resemblance to the gonococcus. Beside their ability to grow upon Loeffler's blood serum or in nutrient bouillon, their behavior upon certain other media merits special remark.

The diagnosis of the gonococcus appears to rest essentially upon the exclusion of the other similar diplococci. Following the researches of Neisser, Steinschneider and others, it has come to be generally accepted that the gonococcus, beside being always decolorized after Gram's stain, is capable of growth only on media containing proteids, *i. e.*, blood serum, ascitic fluid, hydrocele fluid, etc. The differential diagnosis between *Micrococcus catarrhalis* and *meningococcus*, from sources other than the spinal canal of patients suffering from meningitis, is still somewhat uncertain. The chief points of difference so far brought forward are slight, being purely cultural and dependent upon appearance of growth and

* The micro-organism isolated from the third case is of course disregarded here, since study of its cultural characteristics was not carried out.

of colonies; and these characteristics are moreover admittedly variable and cannot fail to be modified to a greater or less extent by fluctuation of conditions pertaining to the medium employed. Further, it is extremely probable that the specific name *Micrococcus catarrhalis* has heretofore served to cover not one species, but all the members of an uncertain group of Gram-decolorizing diplococci, (which are neither gonococci nor meningococci).

Attempts at differentiation by means of specific agglutinative sera have yielded uniformly unsatisfactory results in the hands of others as well as ourselves; and up to the present time, there has been reported no procedure which renders agglutination tests applicable for this class of micro-organisms. For these reasons, any means of ascertaining the species to which any particular culture belongs has a definite value.

During the past twelve months, all cultures of Gram-negative diplococci obtained by us from whatever source have, at Dr. Norris' suggestion, been inoculated into the various carbohydrate-serum-water media, in the hope of obtaining from a classification of their reactions some means of identifying the various members of this morphological group. The reactions obtained have been extremely uniform for each species, except the so-called *catarrhalis*, and have resulted as follows:

The meningococcus has invariably produced an acid reaction in litmus-dextrose-serum-water, and in maltose-serum-water in the course of three or four days, without bringing about any apparent change in any of the others of the series of carbohydrates ordinarily used. Recently, before this Society, Dr. Dunham has reported the same observation with reference to cultures of meningococcus isolated from spinal fluids.

The few strains of presumably true gonococci which we have thus tested have never produced any change which could be recognized with litmus. These cultures have been derived from cases of vulvo-vaginitis in children, from cases of suppurative oöphoritis. etc.

The cultures taken to be *Micrococcus catarrhalis* have varied in that some of them have not fermented these media, while others have acidified dextrose and maltose, and furthermore, have coagulated saccharose-serum-water within 24 to 48 hours. These cultures included several kindly sent us by Dr. Libman, from Mt. Sinai Hospital.

Meningococcus, therefore, gives in these media, a definite reaction which serves to distinguish it from others of the group of morphologically similar Gram-decolorizing diplococci.

In accordance with this routine method, the cultures isolated from these infected joints were tested upon the sugar media. In spite of other apparent resemblances, the various strains described did not behave alike when grown upon these media.

The cultures from Case I, obtained from two aspirations, produced a distinct acid reaction in litmus-dextrose-serum-water, after four to five days, and in maltose-serum-water after a somewhat longer time. On the other hand, cultures from cases II and IV produced no apparent change in the serum sugar media.

A complete review of the literature of this subject will not be attempted in this paper. A few reported cases, however, may be cited.

Wadsworth has reported the isolation of a Gram-decolorizing diplococcus from the knee-joint fluid in a case of scarlet fever.

In Mallory and Wright's *Pathological Technique*,

3rd Edition, 1904, the following statement is made: "In proof of the necessity of cultures for confirming the identity of the gonococcus in certain instances, we may state that we have met with a Gram-decolorizing coccus in an arthritis of the knee, clinically of gonorrhoeal origin, which, in cover-glass preparations from the exudate, was regarded as the gonococcus, but which was found not to be that organism by the study of it in cultures." No further description is given, and we do not know whether the case has been reported in detail.

Gwyn, in the *John Hopkins Hospital Bulletin* for 1904, reports the finding of the *Diplococcus intracellularis* of Weichselbaum, in the spinal fluid, in the circulating blood, and in the knee-joint fluid, in a case of epidemic cerebro-spinal meningitis.

Evidence of pathogenic action of these micro-organisms in our cases is based only upon their presence in the joints and in the general circulation. These cases, however, illustrate the importance of the cultivation of the Gram-negative cocci, no matter where present—urethra, joint, etc.—through numerous sub-cultures before reporting them as gonococci. This fact has not been emphasized, and its importance not generally recognized.

The association of joint affections arising from infection with cocci other than the gonococcus with specific or non-specific urethritis, assumes further practical importance in judging of the benefits of treatment with anti-gonococcus serum, since, without bacteriological examination in these cases, no accurate conclusions can be drawn as to the value of such treatment.

Discussion.

DR. E. LIBMAN said that he was very glad that Dr. Flournoy had brought this subject up for discussion.

There was great difficulty in classifying these organisms. In a paper which he would shortly publish he had mentioned that he had found an organism, which was Gram negative, in the blood post-mortem, which grew with a pink color in certain media. In another case, of otitis media, Gram negative diplococci were found which fluidified gelatin and produced an odor. In these cases it was difficult to say anything about the identity of the organism. The question might come up as to the possibility of a change in the cultural characteristics of the gonococcus in a new variety of medium. The gonococcus might in a joint take on characteristics which it did not have before. If in all the cases in which gonococci were found in secondary lesions they were carefully compared with gonococci from the urethra we might learn whether changes may occur in its biology. It was known for instance that the colon bacillus varied in different parts of the body, especially in the bile. There seemed to be a great variation in the growth of bacteria according to their source. A number of authors had described the growth of gonococci in various media other than those containing human serum. In some studies which Dr. Libman had made he had not found that the gonococcus would grow on agar, no matter what sugar was added. He had therefore concluded that an organism growing on agar should not be considered as a gonococcus; but several authors have described the growth of the gonococcus on agar.

DR. FLOURNOY said that the question as to whether or not a change might occur in the cultural characteristics of the gonococcus isolated from sources other than the genital tract would be hard to settle since we had only cultural tests by which to distinguish the gonococcus.

A CASE OF ANTHRAX OF THE PLEURA.

J. E. WELCH, M.D.

This patient, a male, aged thirty-seven, a Russian by birth, was admitted to Ward 19, Bellevue Hospital, on July 16, 1905. He was a laborer by occupation. The family history was negative and his habits were good. Nine years ago he had pain in the chest and a cough which lasted for one week. Two years later he had a similar attack which lasted two weeks and confined him to bed. Two years after this he had a third attack which involved both sides, but was not very severe. For the past seven years he has had more or less cough.

Two months previous to admission to the hospital he noticed a pain in the left side while doing heavy lifting. After this he noticed shortness of breath and general weakness. These symptoms grew steadily worse until he was compelled to enter the hospital.

Physical examination on entrance showed a man of medium build, swarthy complexion, fairly well developed; skin hot and dry; mucous membranes pale; lips cyanosed; respirations increased and short; chest expansion generally diminished; extraordinary muscles of respiration brought into play; epigastric pulsation present; breath fetid. Apex beat of the heart not definitely located; sounds not distinct. Examination of the lungs gave signs of bronchitis on the right side. Over the left lower lobe the vocal fremitus was increased and there were cavernous breathing and marked increase in the vocal sounds. There were many large and small moist râles heard over the upper lobe and anteriorly there were dullness, increased vocal fremitus and resonance. The remaining part of the physical examination revealed nothing abnormal. The temperature on admission was 103.5°. Subsequent variations are shown on the temperature chart.

The urine was clear, amber, acid, specific gravity 1.025; no albumin; no sugar; urea, 9 gr. per oz. The microscope showed a few hyaline casts. The sputum showed a few diplococci. No tubercle bacilli were found.

Postmortem examination was made twenty-four hours after death. Inspection showed a man as described in the physical examination. There were no pustules or inflammatory areas noted on the skin surface or about the mouth. Section of the thorax only was allowed. There was no special change in the gross appearance of the heart. The right pleural cavity had many old adhesions through it. There was no fluid present. The right lung showed slight anthracosis and emphysema. Section showed congestion and muco-purulent bronchitis. The left pleural cavity contained about two liters of fluid which contained a large amount of fibrin. The pulmonary and parietal pleura was covered by a thick layer of fibrin. The left lung was very much diminished in size from pressure of the pleural fluid. The pleura covering it was much thickened and throughout it contained many small abscesses very circumscribed and circular, averaging in diameter about three mm. There were no abscesses seen in the lung tissue.

Microscopic examination of the lung showed collapse of the air spaces. There was extensive round cell infiltration about the bronchi and they contained pus and desquamated epithelium. The pleura showed many abscesses and an exudate of fibrin.

A culture made in broth from one of the abscesses showed a pure growth of anthrax. Two c.c. of the culture injected into a small rabbit caused the death of the animal in eighteen hours. The bacilli were found in the tissues of the animal and showed a growth identical with the original culture.

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DR. F. S. MANDLEBAUM, *President*.

CASE OF OBSTRUCTIVE JAUNDICE AND BICHLORIDE POISONING.

F. C. WOOD, M.D.

Dr. F. C. Wood demonstrated sections from the organs of a case of chronic jaundice due to the formation of calculi in the bile ducts of the liver, with calcification of the kidneys induced by the action of bichloride of mercury.

Discussion.

DR. W. B. NOYES asked whether the deposit of calcium was to be considered an acute process. He had always considered it a chronic and long continued process, but Dr. Wood's statements suggested that it was extremely acute.

DR. WOOD said that the calcification ordinarily seen was, of course, a chronic process; but one could get a lesion in rabbits in from two to five days, by injecting about five centigrams of bichloride. The rabbit's blood had a large amount of calcium salt in it which made the replacement very rapid. In his own case he could not say that the lesion was produced so rapidly, but the symptoms of the poisoning were very acute. Dr. Hodenpyl's case was ill only five days and the lesions were pretty well advanced, though not so far as in the case shown.

DR. CHARLES NORRIS asked whether there had been any colitis in this case.

DR. WOOD said that no very extensive lesions were found in the intestine. The gut was examined and was found to be very much congested and slightly necrotic on the surface, especially in the colon. There was also a very marked gastritis and the stomach contained a great deal of mucus, but there were no ulcers. The duodenum was intensely congested, more so than the rest of the intestinal tract. The only possibility of the poisoning seemed to be through the infusion fluid, which would have put the bichloride directly into the blood.

DR. HARLOW BROOKS asked whether the calcification of the kidney tubules was characteristic of bichloride poisoning.

DR. WOOD replied that it was said to be so. It had been described in experimental work only in connection with sublimate poisoning and artificial nephritis in animals. Cases of bichloride poisoning had practically all shown calcification of the kidneys where sufficient time had elapsed for the complete development of the lesion. The condition was easily and constantly produced in rabbits by the injection of bichloride.

AN UNUSUAL CASE OF SYRINGOMYELIA.

M. G. SCHLAPP, M.D.

Dr. M. G. Schlapp presented a rather unique case of syringomyelia which had been under his observation for about a year, and on which he had made a diagnosis of an extramedullary spinal cord tumor and suggested an operation. The patient was a man, forty-three years of age, a Scotchman, and a carpenter by trade. His father was living and eighty-two years old. His mother died of Bright's disease, aged seventy-five years. He had four brothers and three sisters all in good health. There was no history of family disease or of deformities. The patient had been in the United States for seventeen years, and had worked until one year ago. He was married and had four healthy children. He had never used alcohol or tobacco. As a child he had had scarlet fever, measles and whooping cough. From childhood until about ten years ago he enjoyed good health. About ten years ago he noticed that at times he had some difficulty in starting the flow of urine. One year later there was a sudden onset of severe pain in the lumbar region of the spine. A week later, there was weakness and numbness of the legs, but not complete paralysis. Any jolting at this time would intensify the pain. The left leg recovered in a few weeks. The patient was incapacitated for three months by the pain in the right leg. At the end of this time he resumed work, using the right leg with special care as any jar caused intense pain. Four years after he was again laid up with an acute attack of pain. About eighteen months ago, that is, about five months before coming to the Dispensary, he had an attack of pain in the lumbar region and in the right leg. Since this last attack he had been unable to return to

work because of pain and weakness in the right leg. The retardation of urine increased. There was also a slight loss of rectal control. The patient had not lost weight; his appetite was good and his pulse regular. He complained especially of weakness and partial loss of power and of pain in the right leg. There was anesthesia over the anterior and lateral portion of the right leg. The area of anesthesia as shown by the photograph corresponded to the area supplied by the 1st, 2d, 3d, and 4th lumbar sensory roots. There was a spastic condition of both legs. There was ankle clonus on the right side always and on the left side only at times. Babinski's reflex was constantly present on right, inconstant on left leg. The cremaster reflex was absent on the right side, diminished on the left. The abdominal reflex was absent on the right side, diminished on the left. The reflexes were normal in other parts of the body. There were no muscular atrophies. The condition existed for eighteen months and in that time the progress of the symptoms was very slow. Operation was advised as it was thought that the patient suffered from an extramedullary tumor involving the 1st, 2d, 3d, and 4th lumbar roots on the right side of the cord.

At operation, however, no tumor was found. Dr. McCosh exposed the cord, taking away the 10th, 11th and 12th dorsal arches. It was found that there was a slight adhesion on the right side between the dura and pia at about the 1st and 2d segments of the lumbar region. Immediately after operation the patient was completely paralyzed from the 12th dorsal segment down. There was an absolute loss of all sensation on the right side, though there was still slight sensation left in the left leg. The sensation in the left leg continued for two weeks and then entirely disappeared, and complete par-

alysis continued until his death. About a week after the operation he developed bed sores. During the last two weeks of his life he developed symptoms of infectious meningitis which had evidently spread from the bed sores, as these contained very much pus.

At the autopsy, which was performed by Dr. Tuttle, nothing special was found in the organs. Around the lower portion of the spinal cord there were large pockets of pus which spread out from the indurated tissue at the site of the bed sores. Nothing could be seen on the outer surface of the cord except the meningitis. There was nothing in the brain. After the brain and cord were hardened, transections were made through the cord about 1 cm. apart and a very interesting condition was found. The patient had a gliomatosis throughout the whole length of the cord. That lesion was very marked throughout the whole cervical cord and yet the patient had shown no symptoms of involvement of any part of the cervical cord. On going further down in the dorsal part of the cord, it was found that the gliomatosis increased in size and involved not only the right but both the right and left side. About the 9th dorsal the whole picture of a gliomatosis was erased by what appeared as a mass of pus, but which on section was found to be a very peculiar tumor. This tumor existed over an area of about two or three segments. It was of the type called neuroepithelioma. Below this tumor the gliomatosis was again found taking its position in the region of the right posterior and middle root zones. The clinical manifestations of the loss of pain, temperature, and tactile sense could be accounted for by this gliomatosis on the right side of the posterior column involving the 1st, 2d, 3d, and 4th lumbar posterior nerves. The neuroepithelioma very likely did not exist at the time of the

operation. The patient could and did walk into the hospital. The only symptoms were loss of sensation over the area mentioned. Otherwise he had no disturbance except the spastic condition of the legs and weakness. The tumor could not have existed at the time of operation because it was of a very rapidly growing type and the symptoms had not progressed rapidly before the operation. The tumor must, therefore, have developed after the operation and in six weeks destroyed the whole of the cord. The operation very likely brought about a disturbance of tissue tension, which in turn caused a changing of the character of the glia cells in this gliomatosis to those of a rapidly growing glioma. The tumor contained a great many cysts lined with ependyma cells.

A similar case had been described by Rosenthal who thought that the cysts were diverticulæ from the central canal. Dr. Schlapp thought his case disproved this and that the cysts developed from the glia cells. Dr. Schlapp thought his case unique in that he felt he could say that the tumor had not existed at the time of operation. Probably the manipulation of the cord at the time of operation and possibly also the hemorrhage which took place had disturbed the tissue tension in such a way as to change the character of the cells in the gliomatosis to rapidly developing glia cells. One or two other cases had been reported which showed this same structure, but the case of Rosenthal was the most similar with the exception that his had existed for a number of years.

Dr. Schlapp expressed his thanks to Dr. Thacher for permission to make use of the material. The case will be reported in full later.

Discussion.

DR. F. C. WOOD asked if there were many mitoses found in the nuclei of the cells of the tumor. Such a

rapidly growing tumor should, in his opinion, show many mitoses. In rapidly growing carcinomata, for instance, in which the rate of increase was no greater than in the tumor shown, enormous numbers of mitoses were often found.

DR. SCHLAPP said that he had not found any mitoses.

DR. HARLOW BROOKS said he thought that one of the most interesting points about the case was the relationship which apparently existed between the unbalanced cells of the gliomatous proliferation around the central canal and the formation of this out and out tumor. The case was of course also remarkable clinically. It was hard to see how the cervical cord could have been extensively diseased and not give rise to symptoms of the most marked character.

DR. W. B. NOYES said that the symptoms, he thought, depended entirely on the length of time and the gradual onset of the gliomatosis. In a great many cases it was practically a very long standing condition, if not congenital, and thus gave rise to perfect opportunity for the tracts to accommodate themselves. There would then be fewer symptoms than in a case coming on in later life and acting more definitely like an eroding tumor. He thought there were two pathological processes here: the syringomyelia with less symptoms than he had ever heard of in so advanced a case; and the sudden change of the tumor, as Dr. Schlapp had explained, in the lower section of the cord with the rapid disintegration of the tracts.

A GLIOMA OF THE BRAIN.

M. G. SCHLAPP, M.D.

Dr. M. G. Schlapp also presented for himself and Dr. Hoobler another case which was interesting clinically and possibly could be brought into connection with the first case. The patient was a man of thirty-five years, born in this country, a blacksmith by trade. He had been perfectly well up to his thirty-fifth year. He gave a history of tuberculosis in the family; otherwise there was nothing in his or in the family history of any importance. Some five months before admission, while bending over shoeing a horse, he suddenly felt a numbness come over his right side. About three minutes after, his right arm, face and leg became weak, and he lost consciousness. He was taken to the hospital and remained in a comatose condition for some time. When he recovered consciousness it was found that his right arm, leg and face were paralyzed. After a time the right leg got better and his right arm slowly recovered. He was in the hospital from the 5th of September to the 10th of December. By that time he could walk around although he limped a good deal. The right arm was rather stiff and the right face was a little weak, but he suffered no special inconvenience. On the sixth day after he left the hospital he again had an attack of dizziness. His right side became weak and he lost consciousness. He was taken to the Presbyterian Hospital where he remained unconscious for about four hours. When he came out his right leg, arm, and face were completely paralyzed, though after he was clear enough to be examined it was found that he had very little sensory disturbance. For some days he felt better and some worse, with vomiting, headaches, and so on. The arm, face, and leg got somewhat better.

About six weeks before his death he became worse; his headaches and dizziness increased. The diagnosis was made of intracranial tumor involving the motor centers on the left side, especially the arm center. As there was very little sensory disturbance it was thought that the tumor spread back. The tumor was localized and the operation performed by Dr. Eliot. A tumor was found which was a large mass filled with a soft bloody substance which was taken out with a spoon. It was very soft and mushy. The whole tumor was not removed. The patient died the next morning.

At autopsy it was found that the man had an enormous tumor lying in the superior frontal convolution and extending back into the precuneus, involving a very large area. There was no reason why he should not have had a very marked sensory disturbance. It was interesting that at the time he had the sudden attack he had no symptoms of an intracranial growth. This attack was unquestionably brought about by a hemorrhage which probably took place in a small tumor. From the time of the hemorrhage until his death the tumor must have grown very rapidly. The hemorrhage probably caused a change in the tissue tension as in the first case, and caused a more rapid growth of the tumor.

Dr. Schlapp also expressed his thanks to Dr. Thacher for the use of this material. The case will be reported in full later.

REPORT OF A CASE OF MELANO-SARCOMA
OF THE BREAST.

E. H. POOL, M.D.

In the case reported below the question of interest is not whether the tumor was primary in the breast, for from the history it is fair to assume that there was an antecedent sarcoma of the choroid. The unusual feature is the long interval which elapsed between the removal of the eye and the appearance of the metastasis. The fact that the recurrence took place in the breast is also unusual.

The patient, a woman, fifty-five years old, was admitted to Dr. Pool's service at the French Hospital on January 8, 1906, and gave the following history, which is taken from the records of the case. She has had four children, the youngest twenty-nine years ago. In 1899, her right eye was removed. The records of the hospital where the operation was performed contain only the following: "Phthisis bulbi; Enucleation; June 10-14, 1899." She could give no definite account of the trouble except that she sought treatment because the eye felt sore. The doctor gave her to understand that the eye was inflamed. It has been impossible to get further facts than the above.

One year ago, *i. e.*, five and a half years after the above operation, she noticed a small lump in the right breast, which has been painful during the past three or four months. Since the pain began she has noticed a considerable increase in the size of the tumor and has lost a good deal of weight and strength.

Physical Examination: Pale, moderately emaciated woman. The skin of the entire body shows absence of pigment moles and other abnormalities. The right

breast is slightly larger than the left; the superficial veins are markedly dilated. One inch below the middle of the clavicle there is a small subcutaneous tumor, one-fourth inch in diameter, hard and adherent to the skin which has a faint bluish color over the tumor. In upper and outer quadrant, about one and one-half inches from the nipple, is felt a mass about two inches in diameter. It is hard, but not so much so as a scirrhus carcinoma, rather circumscribed, movable on deeper parts, not adherent to skin. In the axilla several hard nodes the size of peas are palpable. The left breast is normal. There is no evidence of metastases elsewhere in the body.

Urine examination, negative; no melanin found in a number of tests.

Operation, January 9, 1906: After an exploratory incision into the tumor, the usual complete operation was performed, and the node beneath the clavicle was removed with considerable surrounding tissue.

The wounds healed by primary union and the patient was discharged on the tenth day. She died very suddenly about three months after the operation. The cause of her death was given by her family physician as apoplexy. There was no autopsy.

Pathological Report: The tissues presented at the outer margin of the mammary gland a firm, almost circular encapsulated tumor, about one and one-half inches in diameter. On cut section the growth was for the most part dark brown, elsewhere grey, and was divided into well marked lobulations.

Microscopic Examination: The growth is very cellular. The cells are of various sizes and shapes, round, oval, spindle, and polyhedral. Large spindle cells predominate. The cells lie close together and their outlines are generally indistinct. There is a slight amount of

fibrillar stroma. The cell body is granular and in many places contains pigment granules of a dark brown color. In places the cells are degenerated and appear as irregular masses of pigment. The cells present large, oval nuclei. Mitoses are present, but are not a marked feature. A considerable portion of the tumor is necrotic. It is noteworthy that the pigment cells are seen to be more numerous and darker as one approaches the edge of the necrotic area.

Dr. Pool showed the gross specimen, also microscopic sections of the tumor.

AN UNUSUAL CYSTIC TUMOR OF THE BREAST.

E. H. POOL, M.D.

The tissue removed from each breast was round and flattened, measuring about 10 c.m. in diameter and 3 cm. in thickness. About one-third of the tissue in each mass consisted of fat, the remainder being rather firm, compact, diffuse, grayish tissue containing cysts. In the left breast there were two large cysts, 3 cm. and 2 cm. in diameter, seven about the size of peas, and numerous minute ones. The right breast was slightly more cystic. The walls of the cysts were composed of a smooth membrane. The contents of the large ones was a thin, dark brown fluid; while the smaller ones were filled with thick, mucus-like material. Microscopically sections from the tumor presented many microscopic cysts separated by considerable connective tissue, and filled with a mucus-like substance. The cysts were in general lined with one

or several layers of low cylindrical epithelium, of the general type of that which lines the ducts of the mammary gland. The walls of the large cysts also presented a cylindrical lining. In the connective tissue there was present normal mammary gland. The fluid within the large cysts, on microscopic examination, showed a large number of cholesterin crystals and fat-bearing colostrum corpuscles of the type commonly found in breast tumors. Spectroscopically, blood pigment could also be demonstrated.

MALAKOPLAKIA OF THE URINARY BLADDER.

Report of two Cases.

A. M. PAPPENHEIMER, M.D.

(From the Pathological Laboratory of Bellevue and Allied Hospitals.)

The term "malakoplakia" was first used by von Hanseemann (1) in 1903 to designate a curious disease of the urinary bladder, characterized by the presence in the mucosa of irregular, slightly raised, fungoid plaques of a yellowish color. The first cases of this affection were, however, described by Michaelis and Gutmann (2) in 1902, in an article entitled "Ueber Einschlüsse in Blasentumoren". Since then similar cases have been fully described by Landsteiner and Störk (3), Gierke (4), and Minelli (5). In all ten previous cases have been recorded.

The disease appears to be one of later life, the ages of the subjects varying from forty to seventy years. The majority of the cases have been in females. Including

the author's cases, eight have been found in women, three in men; in one case the sex was not stated. An associated pulmonary or urogenital tuberculosis has been found in five of the twelve cases. In one, the bladder itself showed tuberculous ulcerations, but no tubercle bacilli could be demonstrated in the plaques themselves. The number of cases is as yet too few to decide whether the coincident occurrence of tuberculous lesions in other viscera is more than fortuitous.

The plaques vary in number, size, and distribution. There may be but two or three, as in one of our cases, or there may be several hundred. In size, they vary from small nodules not larger than miliary tubercles to large, flat, confluent outgrowths several centimeters or more in diameter. They are rarely raised more than 1 or 2 mm. above the level of the mucosa. The edges are abrupt or slightly overhanging. The surface is flat; often in the larger plaques somewhat depressed or umbilicated in the center. The color is greyish yellow. Most often, the plaques are set into relief by a vivid zone of hyperemia in the adjacent mucosa. This zone, probably because of postmortem changes in the blood pigment, may appear brown or greyish.

It is difficult to decide from the gross appearance whether the epithelium is continuous over the surface of the plaques. In several cases it has been stated that the epithelium was ulcerated over the center of the plaque; subsequent microscopic examination has then shown it to be deficient over the entire outgrowth.

The distribution of the lesions is highly variable. Sometimes they are most closely aggregated about the fundus, sometimes about the trigonum; most often they are scattered over the entire mucous membrane. In but one case (Michaelis and Gutmann, Case III) have they been found in the ureters and pelves.

There has been a remarkable uniformity in the descriptions of the histological appearances of these structures. Save for minor points, the authors are entirely in accord, and it is only in the interpretation of the lesions that their views diverge.

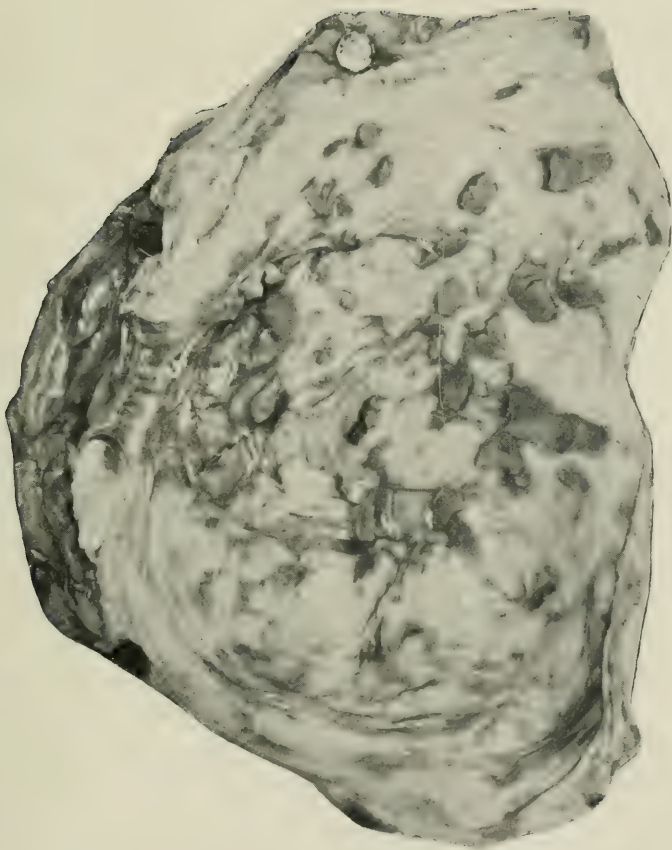
The plaques consist principally of large, oval or polyhedral cells, closely aggregated, with little or no supporting fibrous reticulum. The cells are limited to the mucosa and superficial portions of the submucosa. They are of varying size, but are as large at least as a liver cell. The nucleus is usually eccentric. It may be vesicular, but it is more commonly small and deeply stained. The cytoplasm is strongly oxyphilic, and often presents a foamy or vacuolated appearance. At the base and sides of the plaques there is often a considerable amount of infiltration with lymphoid cells. Small round cells are also scattered amongst the large cells in the plaques. The surface of the plaques is invariably denuded of epithelium, and no transition is to be observed between the epithelial cells at the margin of the plaque and the large, polygonal cells of which the plaque is composed. Blood vessels are quite abundant, and consist of thin walled capillaries, most often directed vertically.

Emphasis has been laid by all writers upon certain hyaline, spherical bodies, wrongly termed "inclusions" since they occur both within and without the cells. These bodies vary from just visible granules or droplets to large, concentrically ringed structures, four or five times the size of a red blood corpuscle. They stain readily with aqueous hematoxylin, without previous mordanting, and give a distinct Berlin-blue iron reaction with potassium ferrocyanide and HCl. According to Gierke, they also give micro-chemical reactions for calcium. Their nature and significance have been the subject of considerable

discussion. They are supposed to be derived from broken down red corpuscles directly by Landsteiner and Störk (3), or indirectly from indigested blood pigment by Minelli (5).

Bacteria have been found in the plaques and commented upon by all the writers except Michaelis and Gutmann. They are found in clumps or colonies, in the deepest portions of the plaques as well as in the more superficial. They are frequently intracellular. Morphologically they resemble the colon bacillus. With Gram-Weigert's stain they decolorize more or less readily. They are not acid fast. Cultures have never been made and the nature of the organism is quite unknown. By Landsteiner and Störk the bacteria are thought to be of etiological importance; by von Hansemann, Gierke, and Minelli, they are regarded merely as possible, and by no means specific, incitants of the disease.

Concerning the nature of the process, whether inflammatory or neoplastic, the final word has not been said. Gutmann and Michaelis, basing their opinion upon the faulty observation that the large, polygonal or ovoid cells were derived from the epithelium, considered the lesion as a form of benign epithelial neoplasm. Their third case, in which the plaques extended to the ureters and pelves, they considered as a more malignant variety of the process. All the other writers, save von Hansemann, who does not commit himself to a definite opinion, consider the lesions as infectious granulomata of inflammatory origin. The precise origin of the characteristic large cells is still a subject for speculation. That they are of similar origin to the phagocytic cells seen in other inflammatory processes seems beyond question. Their large size may, as has been suggested by Minelli, be due to the imbibition of fluid from the urine.



Photograph of Inner Surface of Bladder.

Two cases of this infection have been found in Bellevue Hospital during the past month. The first case was in a woman, sixty-four years old, who died shortly after admission to the hospital. The autopsy was made forty-three hours after death. Her bladder showed a few greenish colored, freely movable, superficial nodules, varying in size from 2 to 4 mm., situated on the posterior surface near the fundus. The trigonum was free. There was a moderate general cystitis, the cavity of the bladder containing slimy, whitish muco-pus. Microscopical examination of these plaques showed a characteristic histological picture, with large cells, very numerous hyaline "inclusions" giving the iron reaction, and numerous colonies of bacilli, somewhat longer than the colon bacillus, but having the same distribution and tinctorial reaction as those hitherto described.

The second case was also in a woman, fifty-three years of age, with advanced pulmonary and intestinal tuberculosis. The autopsy was made four days after death. The bladder exhibited is taken from this case. The mucous membrane is studded everywhere with the plaques, abrupt, raised 1 or 2 mm. above the surface of the mucosa. The color is yellowish or yellowish green. About the plaques there is the usual zone of hyperemia. In the region of the trigonum the plaques are confluent, completely surrounding the ureteral orifice. The size of the individual plaques varies from 1 mm. up to 2 or 3 cm. They are most numerous on the trigonum and on the posterior wall. The surface of the plaques is covered with a small amount of greenish exudate, which can be scraped off. The bladder wall is not apparently changed, and the mucous membrane is elsewhere entirely normal. Histologically, the characteristic structure is obscured, partly by postmortem changes in the tissue, partly also by

inflammatory infiltration and necrosis. The characteristic "inclusions" giving the iron reaction could not be demonstrated, nor were the bacteria, which have been present in all previous cases, to be found. Since, however, there is no other known bladder lesion presenting a similar macroscopic appearance, the lesion must for the present be classed as one of malakoplakia.

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THE PATHOLOGICAL ANATOMY OF THE THYROID GLAND IN GRAVES' DISEASE.

JAMES EWING, M.D.

During the past winter I have had opportunity to examine the thyroid gland in some thirty cases of Graves' disease, and the viscera in five fatal cases. This material has been supplied to me by the Doctors Mayo, of Rochester, Minn., and by several of my colleagues in this city, to all of whom I take pleasure in expressing my sincere thanks. The main objects of the study have been

to determine whether there is any specific difference in the histology of the exophthalmic from that of the simple goitre, and what basis the histology of the thyroid offers for the theory that Graves' disease is chiefly due to hyperthyroidization. In the thyroids studied the lesions seem to fall into four histological groups which also appear to be parallel with four clinical types or stages of the disease.

1. Simple hyperemia with slight excess of soft, poorly staining colloid. These glands occur in early stages of the disease with slight enlargement of the thyroid.

2. Hyperemia, moderate cellular hyperplasia, and excess of poorly staining colloid. Such glands occur in many well marked cases of Graves' disease which have not been of very great severity or of very long duration.

3. Extensive cellular hyperplasia with marked diminution or absence of colloid. These changes are seen when the disease has long been active, and the symptoms pronounced and sometimes urgent or fatal. Such changes, however, may develop more rapidly in toxic cases.

4. Extensive cellular hyperplasia with little colloid, and with fibrosis, hyaline degeneration of stroma, arteriosclerosis, hemorrhages, and cyst formation. These lesions appear in prolonged cases which tend to run into myxedema.

While the majority of these histological features may be seen in simple goitre, the general tendency in Graves' disease is toward excess of cells, while in simple goitre the predominant feature is excess of colloid. There are some characters in the Graves' goitre which appear not to occur in the simple goitre. One of these is the presence of areas of densely packed alveoli free

from colloid, lined by actively multiplying cells, or of diffuse areas of large cells among which are many giant cells. Diffuse infiltration with round cells is also a sign of active thyroiditis, which is rather characteristic of Graves' disease. On the other hand, Graves' symptoms appear to develop in any type of goitre, even with malignant tumors. The histological distinctions are not of fundamental importance, since simple goitre is a condition very closely related to Graves' disease.

The theory of hyperthyroidization is strongly supported by the histology of the Graves' thyroid, since this series of changes is comparable to similar processes seen in other tissues, which have always been interpreted as signifying functional hypertrophy. The theory is also supported by most of the prominent facts of the disease: by the effects of overfeeding of thyroid substance, which aggravates Graves' disease while curing its counterpart, myxedema: by the therapeutic results of partial extirpation of the enlarged gland: by the aggravation of the symptoms following massage of the gland: by the physiological effects of administration of the active principle of the gland, iodothyrim, especially the similarity in the metabolic disturbances in Graves' disease, and after the use of iodothyrim: and, finally, by the results of chemical analysis of the diseased thyroid.

The histology and chemical analysis of the thyroid do not satisfactorily explain all the clinical features and type of the disease. In the earlier stages and in many acute toxic cases the histology of the gland offers sufficient basis for the theory that the system is flooded by excessive thyroid secretion. In these cases the extremely hyperemic gland contains an excess of poorly staining semifluid colloid, and evidences of active secretion of

colloid are prominent. In the very cellular glands, however, which may go with severe symptoms, the colloid is deficient and the histological evidences of excessive discharge into the system are inadequate. Possibly in such cases more fluid iodothyroglobulin is discharged immediately into the vessels, as some claim, or the gland may have been very rapidly drained of colloid, or more careful clinical study may show that the excessive nitrogenous metabolism of the early stages of the disease is wanting when the glands are deficient in colloid and iodothyrim. This last hypothesis is suggested by the tendency of the prolonged cases of Graves' disease to exhibit symptoms of myxedema. The theory of hypersecretion, therefore, appears somewhat inadequate for this group of cases, but the functions of the thyroid are probably complex, and overactivity of the gland may be found to include other functions beside that of elaborating iodothyrim.

The parathyroid glands have been implicated in the causation of Graves' disease by some recent writers. In about a dozen cases these glandules have been examined and such changes as degeneration of the cells and fat invasion with replacement of alveoli have been described. In two fatal cases I found the glands normal; in one the cells were clear, pale staining, and apparently degenerating; while in a fourth case there was moderate fat invasion with normal parenchyma. All of these changes occur in cases not suffering from Graves' disease so that no special importance can at present be attached to them. In a series of about one hundred parathyroids in various diseases, collected by Drs. Ferguson and Rogers, the range of alteration has been greater than that described in Graves' disease.

The thymus is persistent and hypertrophic in about

one-half, according to Hansemann, of the fatal cases of Graves' disease. Persistent hypertrophic thymus and other signs of *constitutio lymphatica* were present in all the fatal cases (5) that I have examined. This fact is of interest not only for the pathogenesis of Graves' disease, but for the nature of *constitutio lymphatica*.

The hypophysis has been studied in exophthalmic goitre on account of its considerable content of iodine and the changes which occur in it after extirpation of the thyroid. The results at present do not appear important.

Lesions in other organs arise in the course of all prolonged cases of Graves' disease. These include hemorrhages, degeneration, fibrosis, and atrophy of tissue in the sympathetic ganglia and trunks, vagus, spinal cord, medulla, and brain, all of which appear to contribute toward the nervous symptoms and the permanence of the disease. In many cases there is an anemia of somewhat specific type. There may be a peculiar and extreme fibrosis of the adrenals. Chronic congestion, sometimes associated with productive inflammation of the liver and kidney, may result from the long disturbance of the circulation and metabolism. The enlarged heart may show chronic myocarditis, valvular lesions and coronary arteritis. In one acute fatal case I found an active diffuse myocarditis with edema and extensive infiltration by round cells. Such lesions, together with the active thyroiditis with round cell infiltration, acute degeneration of the liver and kidneys, hyperplastic splenitis, hemorrhages in the medulla, associated with high fever, delirium, and convulsions, demonstrate the extremely toxic nature of these forms of the disease, and the inadequacy of any theory based on an intrinsic neurosis.

Discussion.

DR. F. C. WOOD said that it might interest the Society to know that he had recently had the opportunity to examine the thyroid gland of a dog who had the symptoms of Graves' disease. The lesions were those of the highly cellular type described by Dr. Ewing. The gland structures looked exactly like those seen in human cases of exophthalmic goitre, and the sections could not be distinguished. Dr. Wood asked Dr. Ewing whether he had got any records as to the relative proportion of the enlargement of the thymus in thyroid disease.

DR. EWING said that he had searched the literature for detailed reports of pathological studies of Graves' disease, and had found enlargement of the thymus mentioned from the earliest time, first by Markham in 1827, and probably in more than half the cases. He had himself seen a dog with exophthalmos and tachycardia, but without distinctly enlarged thyroid. Cases of the disease in both dogs and cattle had been recorded.

DR. CHARLES NORRIS mentioned that the three cases which had come to autopsy in his laboratory all had enlarged thymus and very marked *constitutio lymphatica*.

DR. F. S. MANDLEBAUM said that only the day before he had the opportunity of examining a case of this sort. The gland had been removed at operation and he would be very glad to contribute it to Dr. Ewing's collection. Several of the types which had just been described were embodied in this gland. One part was of the cellular type with very little colloid; in other parts the growth was rather diffuse, in one place distinctly adenomatous. Another part showed papillary outgrowths into the alveolar spaces. The outline of the adenomatous

part was not distinct, and it ran into the papillary and cellular types of structure without any definite arrangement or any limitation by a capsule.

STUDIES IN HYDROPHOBIA.

ANNA W. WILLIAMS, M.D.

In a paper by Dr. Lowden and myself on the etiology of hydrophobia, which is still in press, we have showed in the summary of the literature up to that date that the principal points against the protozoan theory of the cause of hydrophobia are the following:

1. In some cases proved by animal inoculation to be rabies, notably in cases of "fixed virus" infection, no "Negri bodies" or other protozoan-like forms have been found.

2. No protozoan-like forms have been found in the salivary glands or in the peripheral nerves, and none have been found in the central nervous system until some time after the tissue has become infective.

3. No forms small enough to pass the coarser Berkefeld filters have been seen, though the filtrates are virulent.

4. Certain forms which have been demonstrated in the large ganglion cells of the central nervous system late in the disease, the so-called "Negri bodies", have not showed a structure or developmental cycle analogous to that of known living organisms.

In our work we feel that we have brought forward sufficient evidence to prove that these points no longer

hold; that is, we have found protozoan-like forms in every case of hydrophobia studied, about 150 in all, including 15 cases of "fixed virus" infection; further, we have found such forms at every stage of the disease, beginning with the time the tissues become infective; also, we have seen forms tiny enough to pass the coarser Berkefeld filters; and, finally, we have found that the structure of all these forms resembles that seen in the growth and multiplication of known protozoa.

In continuing our studies on the more minute characteristics of these protozoan-like bodies, called tentatively for the sake of convenience *Neuroryctes hydrophobiæ*, all of our previous work is being corroborated and certain new points are being brought out.

There are two general distinctive characteristics of these bodies which differentiate them from bodies produced by degenerative changes. First, their refractive quality; this gives them in both smears and sections an appearance of depth which is very characteristic. In smears this is well brought out with the Giemsa stain. Second, their structure, which is extremely delicate but very definite. It is so delicate that unless the smear or sections are very well made the small forms are not seen at all and the structure of the large forms is distorted so that they may have the appearance of degenerations. The bodies have this characteristic definite appearance whatever the animal inoculated and whatever the site in the central nervous system. Important variations occur only with the rapidity of the disease, that is, with the age of the lesion, the variations corresponding exactly with the variations in the growth and development of known organisms.

When we can follow definitely in the hanging drop the different stages of growth and multiplication of a

well-known organism such as the *Amoeba proteus*, the *Plasmodiophora brassicæ*, or the malarial organism, and when we can fix and stain the organism at any stage so that we can come to know the appearance of every stage under these artificial conditions; then, when in different diseases in tissues fixed and stained in the same way we find bodies which present a complete series of forms corresponding more or less closely with the series of forms in the development of the known organisms, we have as definite evidence that we are dealing with a similar organism as if we followed its movements in the hanging drop. We all know what the study of the hanging drop means, that even here we must be educated to see movement and structure.

I have been told that when one crescent is found in a smear of blood the diagnosis of malaria may be made, and with a well brought out crescent in a good smear it seems quite legitimate to make this diagnosis though it might be extremely difficult for beginners in the study of this group of protozoa to make it.

In regard to the neuroryctes, at this stage of our study, we may make just the same statement. In a well made, well stained smear, a body showing refractive qualities, a homogeneous ground substance taking basic stains lightly, an entire margin, and the delicate definite structure of one of the larger forms with its chromatin-staining central body which is definitely structured (the chromatin is a more or less granular ring around an eccentrically situated karyosome and with its secondary chromatin bodies arranged in a more or less complete circle about the central body), if we see such a body situated within the cytoplasm of a nerve cell or between the fibrils of one of its branches, we can say without hesitation that it is a neuroryctes and that the animal containing it was suffering from hydrophobia.

Further, we may say that such a form in its delicacy and regularity of structure is as distinctly a part of a definite life cycle of a living organism as is the rosette form of a malarial organism. With a little more study we may be able to say that one form of any stage in its development is the organism; but fortunately for practical use we do not need to do this because the cases which come to us for diagnosis, with the exception of a very small per cent., have the disease so well advanced that many of the large forms are present.

Of course it is only after we have spent these years of study on the disease and have examined many controls, that we feel we know the points already mentioned, and that we are willing to place these bodies with the protozoa.

The following chart has been made in order to bring out more clearly where we have found our analogies. The organism is not yet definitely classified. It may belong to any one of several groups, but as none of these groups have been minutely studied, its exact place, even when we come to know it fully, may not be determined for some time.

The Ciliophora need not be considered; but when we come to the divisions of the other groups we immediately find difficulties. Many of the Amoebina and Mycetozoa under the Rhizopoda resemble closely many of the Microsporidia under the Sporozoa, and it is in these three groups that we find our closest analogies. The other two groups of the Sporozoa, the Coccidia and the Hemosporidia may be dropped out, as the forms which we have found give evidence of continuing to reproduce during the entire vegetative phase. Our first analogy is with the *Amoeba proteus*; the different phases of its life cycle as described by Calkins, its primary and secondary

nuclei with their fragmentation and distribution throughout the cytoplasm, then, according to surrounding conditions, its breaking up into tiny swarm spores or its rounding out into cyst forms—all are similar in appearance to these forms of the *Neuroryctes*. The free moving *Amoeba* would naturally have well developed pseudopods, while the *Neuroryctes*, parasitic in more solid media, would not. The budding forms are exactly similar to those depicted by Schaudinn in the rhizopod *Leydenia gemmipara*.

The *Mycetozoa* are supposed to be *Amoebina* modified in various ways by parasitism. In this group we have still closer analogies. In *Plasmodiophora brassicæ*, the arrangement of the chromatin in the central bodies and the definite ring of secondary nuclei are quite similar to that seen in the *neuroryctes*. We have in the latter forms apparent fusion of tiny forms similar to the plasmodial stage in the *Plasmodiophora* and a number of other *Protozoa*. If it be true that they fuse in this way such fusion may take the place of definite conjugation.

In the *Mycetozoa* as a group, as well as in other rhizopods, we know that at any time during the stage of multiplicative division, when the conditions become unfavorable to growth, the tiny merozoites or swarm spores may encyst, and we may get in this way one, two, or a group of tiny spores. This may happen with the *Neuroryctes*. The small swarm spores may pass down the nerve fibrils to the end organs and so into the secretions where they may round out and encyst. Such tiny encysted forms, if they exist, may only be demonstrable with difficulty, if at all. This may be the reason why no characteristic forms have been found in the salivary glands or in the saliva.

Among the *Microsporidia* we have a very close anal-

ogy in the *Nosena lophii* of Doflein. This form is especially interesting because it is parasitic in the ganglion cells of a certain fish, the *Lophius piscatorius*. The forms first infecting the ganglion cells are exactly similar to the forms of the *Neuroryctes* seen in the early stages of infection. There are the forms with a tiny chromatin central body, and forms showing different stages of fragmentation of the chromatin bodies; then there are groups of small daughter organisms.

I have not time now to go into more details in regard to these analogies. Suffice it to say that the more varieties of Protozoa and the more cases of hydrophobia we study the closer our analogies become, and if the statements mentioned in the first part of this paper hold we may surely be able in the near future to demonstrate the protozoan nature of the structures to the minutest detail.

CHART.

Phylum: Protozoa	{ 1	Subphylum: Plasmodroma.			
	2	" Ciliophora.			
			{ 1	Order: Amoebina—	
			2	" Heliozoa.	
			3	" Radiolaria.	
			4	" Foraminifera	
			5	" Mycetozoa—	
Subphylum: Plasmodroma	{ 2	" Mastigophora.			
	3	" Sporozoa.			
Class: Sporozoa	{ 1	Subclass: Telosporidia.			
	2	" Neosporidia.			
Subclass: Neosporidia	{ 1	Order: Cnidosporidia.			
	2	" Sarcosporidia.			
Order: Cnidosporidia	{ 1	Suborder: Myxosporidia.			
	2	" Microsporidia—			
Suborder: Microsporidia	{ 1	Tribe: Oligosporogenia.			
	2	" Polysporogenia.			
Tribe: Polysporogenia	{ 1	Family: Nosematidæ.			
	2	" Plistophoridæ.			
	3	" Cytoryctidæ.			
Family: ?		Genus: ?			
Genus: ?		Species: <i>Neuroryctes hydrophobiæ</i> ,			

A RAPID METHOD FOR THE DETECTION AND STUDY OF THE NEGRI BODIES IN HYDROPHOBIA.

IRA VAN GIESEN, M.D.

Dr. Ira van Giesen in presenting this subject stated that the method was of real value in the diagnosis of rabies, and had, in his own experience, supplanted all other procedures in the detection of the Negri bodies. The method had the advantage of being simple, rapid, and accurate, free from capricious results and working uniformly. As the whole procedure occupied but two or three minutes, and could be learned after one or two trials by any one even unskilled in laboratory technique, its advantages for the diagnosis of rabies by the presence of the Negri bodies were obvious.

The procedure consisted of two steps: the preparation of a certain form of smear of the central nervous system, and the application of a new staining solution. The important part of the procedure is the preparation of the smear technique, which is valuable not only for the study of rabies and the Negri bodies, but as a method for the study of the normal and pathological histology of the nervous system in general. The speaker had used this particular form of smear method for a number of years in the study of the nervous system, particularly in the investigation of the normal structure of the neuron bodies, and their degenerative changes in a variety of mental and nervous diseases, and was at present attempting to apply this technique to the study of the neurofibrils. If smears of the nervous system are made by the conventional method of preparing blood films, they are of little or no value. If, however, a portion of the gray or white matter about the size of a bird shot is

placed on one end of the slide under the cover-glass and the cover gently squeezed with the ball of the finger so that the tissue is flattened out into a thin layer, and the cover-glass is then shifted across the slide, very beautiful preparations of the neuron bodies with the coarser axonal and dendritic prolongations may be secured.

These "squeeze smears" are particularly valuable in reconnoitering pathological changes in the nervous system and in determining the subsequent plan of technical procedure for the study of sections. In its specific application to the study of the Negri bodies these "squeeze smears", dispensing with the time and trouble of preparing sections, may be fixed while still moist for a few seconds in methyl alcohol, or dried in the air.

The staining of the smears is to a certain extent of less importance for they may be colored by a variety of methods used for the cytology of the neuron body or other methods in use for the staining of blood smears. The staining solution presented by the speaker, however, was recommended because of its rapid and simple application, and the distinction and individual color reaction conferred on the Negri bodies.

The stain is prepared as follows: To 10 c.c. of distilled water add two drops of a saturated alcoholic solution of rose anilin violet and two drops of a saturated aqueous solution of methylene blue diluted one-half with water. It is best to prepare the stain fresh each day. The stain is poured over the smear; the slide held over the flame until the solution steams, then rinsed with water and allowed to dry; and the procedure is finished. The Negri bodies assume a brilliant crimson hue with their chromatin particles colored blue.

Not only is the procedure convenient for diagnostic purposes but it is of material aid in the detailed study of

the structures of the bodies, as for instance as used in the researches of Dr. Williams and Dr. Lowden now in press. The proportion of the dyes to the staining solution may be very easily modified for application in other directions and possibly the mixture may be found useful in staining bacteria, smears of exudates, blood, and the like.

THE INFECTIVITY OF TISSUES AT DIFFERENT STAGES OF HYDROPHOBIA.

DANIEL W. POOR, M.D.

What little I have to say this evening is not based upon work done specifically upon this subject. There has been no systematic effort to interpret the question of the infectiousness of the different tissues in rabies; but from time to time work upon other points connected with this disease has had some bearing upon the question and a consideration of the results obtained may be of some interest, taken in connection with the papers which have preceded.

Some time ago, while working in conjunction with Mr. Atkinson on a comparison in the reduction in virulence of fixed virus by slow and by rapid drying, it was noted that by drying the tissues rapidly in vacuus over H_2SO_4 both the brain and the cord lost practically all the water, *i. e.*, became completely dried in five days. The brain was able to hold its virulence apparently unimpaired by this drying for a period of at least two and one-half months, whereas the virulence of the cord died out with-

in five days. The loss of virulence in the cord was the same when caustic potash instead of H_2SO_4 was used, and also when the material was dried in an atmosphere of pure carbon dioxide. The comparative virulence of the brain and cord was further tested by examining the fresh material in various dilutions. Although these tests were not of any great use in giving absolute values they served to compare further these two portions of the central nervous system. The brain was again found to be much more infectious, even $\frac{1}{5,000,000}$ of a gram in one instance being sufficient to kill, while of the cord $\frac{1}{10,000}$ of a gram was the smallest killing dose noted. In accounting for the marked difference between the brain and the cord, three points should be considered: (1) the difference in the chemical composition of the two, which might account for an organism growing more rapidly in the one than in the other; (2) the nature of the infecting material; and (3) the site of inoculation. The animals used in these experiments were rabbits inoculated subdurally with fixed virus where the infecting material is exceedingly virulent, causing death about eight days after inoculation. Assuming the cause of rabies to be an organism which grows in the central nervous system, spreading from the site of inoculation, one might suppose that in this case the animal might be so quickly overwhelmed by the poison of the disease that there would be no time given for its full development in the lumbar cord, at a distance from the site of inoculation. This idea seems to be borne out somewhat by an experiment which followed, in which the brain and lumbar cord of a young dog inoculated in the sciatic nerve with street rabies were used. Here the infection spread slowly from below upward, the incubation being seventeen days. Equal amounts of the brain and cord were inoculated after having been dried

five days over the H_2SO_4 in vacuus. Here the cord remained virulent, bringing guinea-pigs down in twenty days as against fifteen days for the brain. Experiments have been started to test the other point mentioned, viz., the relative infectiousness of the gray and white matter at the corresponding level of infection, but are not as yet completed.

That infection spreads in the central nervous system by the steady growth of an organism from the point of inoculation, and is not to any extent carried rapidly to distant points by the cerebrospinal fluid, seems evident from the following experiment carried out in conjunction with Dr. Williams. Nine rabbits were inoculated subdurally in approximately the same part of the brain with fixed virus. A rabbit was killed each day and a portion of the horn of Ammon on the side of the brain opposite to that inoculated and of the tip of the lumbar cord were examined for virulence in strong and weak dilution. At the same time Dr. Williams examined adjoining portions from the same locations, microscopically. Approximately the same sized piece of material was taken in each instance and was emulsified with 3 c.c. of salt solution for the strong virus, and this emulsion was still further diluted 1,000 times for the weak virus. Guinea-pigs were then inoculated with these solutions to determine the rate of progression of the virus. The following observations were noted. Up to the third day the tissues examined were not virulent. On the third day, however, which is three days before rabbits inoculated in this way show symptoms, the strong emulsion of the brain was fully virulent and the weak emulsion was also virulent, but killing with an incubation delayed two or three days. The cord was not virulent. On the fourth day the cord

was virulent; the brain in strong solution was fully virulent, and in weak solution nearly so. In the fifth day rabbit, the cord in strong solution killed one of the two pigs after a protracted incubation; the other remained well. The weak solution failed to kill. The brain was fully virulent. It is between the fifth and sixth day that the rabbits begin to show symptoms, which may have some connection with the complete investment of the central nervous system by the veins. The sixth day rabbit showed the cord in strong solution fully virulent, in weak solution non-infectious. The brain was fully virulent in both dilutions. From this time on until the ninth day the results were that the cord in strong solution and the brain in both solutions were fully virulent. The weak dilution of the cord failed to kill. The eighth and ninth day rabbits died of the disease so that it was unnecessary to drown them. The material inoculated was washed during the first few days to remove any virus that might have been carried down from the site of inoculation by the cerebrospinal fluid.

The infectiousness of the cerebrospinal fluid has been tested in only one case, that of a child; but in this case neither small amounts inoculated subdurally, nor doses of 2 c.c. inoculated deep in the leg in several guinea-pigs produced any effect. While the germ of rabies may undoubtedly be carried in the fluid, it seems probable that it does not multiply in it.

The virulence of the salivary glands has been tested as follows: In sixteen dogs the submaxillary was found to be virulent in twelve and non-virulent in four. All of the non-virulent cases were experimental animals in which the incubation was unusually short. Of the twelve found to be virulent, ten were taken from cases of street rabies, and two from experimental cases. In 100 per cent. of

the clinical cases the submaxillary gland was infectious; and in $33\frac{1}{3}$ per cent. of the cases in which the disease was produced experimentally was this the case. The parotid gland was tested in five cases of street rabies and found to be infectious in only one. In all of the five cases the corresponding submaxillary gland was infectious. We may conclude that the submaxillary type of gland rather than the parotid is concerned in the virulence of the saliva and possibly that a short incubation may tend to lessen the virulence of the saliva. No attempt has been made by dilution experiments to test the relative amount of virus in the glands of different cases.

The virus may be extracted from the gland by glycerine, by simply allowing it to stand immersed in the glycerine for a time. The glycerine, usually colored by the hemoglobin and perfectly clear, may be pipetted off and serve as an excellent virus. In some instances, if kept in the ice box, the virus may be preserved for a long time. In one instance the glycerine extract of the submaxillary gland of a dog with street rabies was able at the end of 191 days to kill guinea-pigs with rabies in twelve days. In other instances the virus dried out earlier, probably due to there being less of it originally present in the gland, though changes in the reaction of the glycerine may have had some effect. When a gland is well infected with the virus the glycerine extract, as well as the salt solution extract appears to infect animals more readily than the nerve tissue when inoculated peripherally. In some instances even small amounts given subcutaneously will produce the disease. By using an attenuated extract of the submaxillary I have been able to lengthen the incubation in experimental

animals in one instance to five and one-half months. This supports the histories of long incubation of which we occasionally hear and which have been doubted by some.

In two instances we have tested the pancreas and suprarenal capsule with the result of finding the virus present in the latter in one case.

Numerous observers have found various other organs virulent when examined after the disease had become fully developed. Marie, by injecting large amounts of blood into the legs of a number of guinea-pigs, proved that it may carry virus.

It seems to be the opinion generally held that the virus of rabies travels along the nerve trunk from the infected area to the central nervous system and then travels in it in both directions until the whole is involved, about which time symptoms develop. As the disease progresses it may be carried in the blood to a greater or less extent into the various organs of the body. The salivary glands are probably infected both by the nerves leading from the brain and by the blood.

The study of the manner in which the body is protected against the rabic virus by the Pasteur treatment is a most interesting and important one from a practical standpoint. From work which has been done thus far it would seem that this is done, chiefly at any rate, by the production of a specific body in the blood as in other bactericidal sera. The treatment develops this immune body slowly but even when started late and when the infection is severe, provided it occurs in parts of the body where it travels up the cord and does not reach the brain directly, as in face bites, it is quite regularly successful. On the other hand, in severe wounds of the face the incubation is apt to be so short that infection occurs before

any great killing power has developed in the blood. From work done by others thus far, as well as from certain work being carried on at present at the Research Laboratory, it would seem that sera from a highly immunized animal might be obtained which when injected into a patient may so delay the progress of the virus that the Pasteur treatment used in conjunction with it will become more effectual in these cases.

Discussion.

DR. GARY N. CALKINS who had been invited to take part in the discussion was unable to be present, but, upon request, sent the following statement:

"There is no doubt at all in my mind that these so-called "Negri bodies" are organisms belonging to the protozoa group. I was not prepared to say this, however, until convinced by Dr. Williams' preparations, which leave little to be desired in clearness of demonstration. The nuclear structures were particularly interesting to me, for the several stages that the preparations showed give almost unmistakable evidence of nuclear changes common to rhizopods and Coccidia at certain phases of the life cycle. The cell bodies appeared to have a variable number of chromatin granules in them in addition to a clearly defined nucleus. This is true also in many rhizopod types and the distributed chromatin is the invariable preliminary phase of swarm spore formation. Thus in the marine rhizopod *Polystomella* the nucleus divides repeatedly, and then fragments into many chromatin particles which pass into sexual swarm spores in the distributed condition to be re-collected into small nuclei when the asexual spore grows into a new adult

organism. They ultimately become the nuclei of sexual swarm spores.

"A more direct process is well known in the case of fresh water shell-bearing rhizopods like *Centropyxis* or *Arcella* or *Diffugia*. In the former, for example, the nucleus throws out a number of chromatin granules which form a mass of chromatoid particles about the nucleus and throughout the cytoplasm. Hertwig gave the name chromidien to this extra-nuclear chromatin and Schaudinn and others have shown that this chromidien forms the nuclei of the small amoeboid swarm spores which conjugate either with or without first dividing. Similar phases have been described in various coccidia, such as *Benedenia*, etc. In rhizopods, again, *Paramoeba* shows the same fragmentation of the nucleus and formation of swarm spores which divide by longitudinal fission. I have described the same thing in *Amoeba proteus*. The single nucleus of the ordinary form divides repeatedly by mitosis until there are from forty to seventy nuclei in the cell. These nuclei then fragment and chromatin particles of various sizes are liberated in the cytoplasm. Here they ultimately become small nuclei of swarm spores. This process differs from that in *Centropyxis* or *Arcella*, etc., in that the nucleus first divides a number of times by mitosis and then the daughter nuclei fragment to form the granules. But in *Centropyxis* the chromatin granules are thrown out of the nucleus during the ordinary vegetative phases and the single nucleus persists until swarm spores are formed when it degenerates and disappears.

"In the hydrophobia organism I should say that the distributed nucleus is formed by elimination of the chromatin as in *Centropyxis* and not by nuclear division as in *Amoeba*, *Coccidia*, or *Polystomella*; but I may be mis-

taken in this. The budding forms show that some of the chromatin granules go into the buds and this again is identical with the happenings in *Arcella*. On the whole, the evidence given by these preparations is enough to indicate that a process is going on exactly analogous to that which takes place in the majority of protozoa in which the life history has been made out. I would place the organism in the family *Cytoryctidæ*."

DR. JAMES EWING wished to express his pleasure in listening to these important communications upon this interesting subject. It had seemed to him that while others had claimed the Negri bodies to be the cause of rabies, most of these claims had lacked sufficient basis for a legitimate conclusion. But to-night the results of systematic study had been given, and the detailed morphology of the bodies had been so much more clearly shown than before that the probabilities seemed more distinctly in favor of the importance of the Negri bodies. There appeared to be two distinct methods to pursue in order to establish that a suspicious structure is a protozoon cause of disease. One might consult authorities in biology; and this method had been pursued extensively. In fact, no well known parasite, spurious or genuine, had failed to receive the pronouncement of some well known biologist. If this method were followed logically all the authorities must be consulted, and the opinion of any one could not be taken; but it seemed questionable whether unanimity of opinion could be secured in this way, while otherwise the results would not carry conviction. Considerable importance, however, must attach to the statement of a recognized expert that the forms of the Negri body closely resemble types of known protozoa. The other method, that of collecting all the circumstantial

evidence possible, seemed more likely to succeed. It had been shown this evening that the Negri bodies had a very definite structure, yet this fact could hardly prove convincing to those who were unfamiliar with the structural details of related protozoa, since in some respects at least the bodies resemble degenerative products. Other lines of work would be needed to furnish necessary corroborative evidence. It would be important to determine if there were any relation between the infectiousness of the material and the numbers of the bodies. He had been disappointed to find that Dr. Poor was not ready to commit himself on this point. The demonstration that different forms of the bodies were present at different stages of the disease would be of interest, and this seemed to be true to some extent. Yet in some acute cases no bodies had been found. It seemed necessary to explain the apparent absence of the bodies from saliva and the salivary glands, since, according to the views of Theobald Smith on parasitism, these glands are probably nature's outlet for the parasite. The fate of the bodies in decomposing material remaining infectious might be of interest. All of these problems had received some attention, but the combined results did not yet seem adequate to demonstrate the parasitic nature of the Negri bodies.

DR. D. W. POOR said in reference to the method of smear preparation and staining which Dr. Van Giesen had proposed that he thought this was going to be of very great advantage in the study of the disease. He spoke more as an outsider in this case; but he had frequently had occasion to have animals examined, for diagnosis, which had been inoculated and had died without definite symptoms, and the results had been very satisfactory. It was rather anticipated that this might be so some time ago when Dr. Williams read a paper, and this had been fully borne out by the recent work which had been done.

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DR. F. S. MANDLEBAUM, *President.*

A CASE OF STENOSIS OF THE ARCH OF THE AORTA.

A. M. PAPPENHEIMER, M.D.

DR. A. M. Pappenheimer presented a specimen of stenosis of the arch of the aorta, very similar to a case which he had shown last year. The organ had been taken from a man, a machinist by trade, sixty-four years of age, and an excessive drinker. His previous history was of no significance. He had always been well until a couple of months before his death. He then developed ascites and edema of the legs, and symptoms due to cirrhosis of the liver. This cirrhosis was the only lesion found at the autopsy with the exception of the stenosis of the aorta. The heart was slightly enlarged. There was slight hypertrophy of the walls of the left ventricle.

The valves were practically normal. The ascending aorta was a little dilated. Just below the origin of the left subclavian there was a very tight stenosis of the aorta which appeared on the outside as a constriction; but on the inside there was seen a ridge or diaphragm projecting into the lumen of the vessel. The lumen at this point barely admitted a small pencil; that is, it was about 3 mm. in diameter. The fibrous remnant of the ductus arteriosus entered the aorta at an acute angle just below the maximum point of constriction. Just below this the aorta rapidly reassumed its normal caliber. The collateral circulation in this case was very striking. The internal mammaries were enlarged to the size of a finger, and were very tortuous. All the vessels above the stenosis were markedly dilated, the superior intercostals especially so. Below the stenosis the first pair of intercostals were dilated. As regards the physical signs, there was no note made of the presence of pulsation in the femoral arteries nor of the presence of pulsating, superficial vessels in the upper thoracic region. There was noted in the second space to the left of the sternum a very systolic murmur, which was heard also in the back, in the interscapular region to the left of the vertebral column. A murmur of this character has been observed in a number of the recorded cases.

ABERRANT BILE DUCTS IN THE LIVER.

E. MOSCHCOWITZ, M.D.

These aberrant ducts came to notice in the course of a study on non-parasitic cysts of the liver. In order to understand their significance it will be necessary to give a brief outline of the various steps which led to their

discovery. The histological study of the case of cystic liver left me in doubt as to their origin.

The cysts are discrete and are made up of smaller and larger bile ducts presenting an adenomatous appearance. The spaces contain a clear mucoid fluid. Either one of two possibilities seemed to be in question, first, that they were inflammatory, and second, that they were new growths. Neither of these possibilities however could be reconciled entirely to the histological picture. This led to a fuller study of the literature and at the outset two striking associations of cystic liver were noted: first, that cystic liver was usually associated with cystic kidney; and, secondly, that in an appreciable number of cases both cystic kidney and cystic liver were accompanied by congenital malformations. Further investigation showed that Hildebrant and Ribbert had already noted this association of cystic kidney and congenital deformities, and had thereupon formulated the theory that cystic kidney was also an anomaly and was due to the non-union of the two urogenital stems. All these factors led me to believe that there must be some maldevelopment as the basis of cystic liver as well, and it remained to show what this maldevelopment was. It is necessary to state here that a few observers had already noted peculiar microscopic bile ducts within the acini in cases of cystic liver, which had mostly been explained as active proliferations of new growths. It occurred to me that perhaps these ducts were primary and the congenital malformations in question. In order to prove this it was necessary to show the presence of these ducts in a non-cystic liver. Such an instance I thought might occur in one of two conditions: either in a fetus in which the kidneys were cystic but in which the liver appeared normal macroscopically; or in a fetus that was otherwise afflicted

with some form of congenital anomaly. Through the kindness of Dr. Hodenpyl I fortunately obtained a fetus that presented both these conditions. The fetus was seven months old; both kidneys were intensely cystic; and in addition there were six fingers and six toes and an occipital meningocele. The liver looked apparently normal. Microscopically, however, the liver presented a peculiar picture. The organ was permeated everywhere by numberless, well formed bile ducts, both in Glisson's capsule and in the parenchyma. With the demonstration of these ducts cystic liver could be easily explained.

In the five cases of cystic liver that I have studied, cystic liver appears to be formed either by retention in these aberrant ducts or by inflammatory hyperplasia. Another search of the literature at this point revealed the fact that these aberrant ducts had been noted but twice before, by Kilvington and by Dunger, but neither of these observers had placed any significance on their find. Kilvington found these ducts in the liver of a fetus whose mother died with cystic liver and who had previously given birth to monsters. Dunger found them in the liver of a woman whose mother had died of cystic kidney. These observations are interesting as bearing out the contention that they are malformations.

Aberrant ducts on the surface of the liver are mentioned by Quain. He says that they are occasionally found in the left lateral ligament or in the fibrous cords that bridge the fissures for the umbilical vessels and the vena cava. That even here aberrant ducts become cystic is shown by a search of the literature in which sixteen cases are reported. Their origin as arising from aberrant bile ducts is not mentioned but a careful study of the cases convinces me that this theory is the correct one.

These aberrant bile ducts are easily explained

embryologically as primitive tubes of the entoderm which fail to proliferate into liver cells. A liver in which these aberrant ducts occur may be said therefore to be in an embryonic state. It is interesting to note in this connection that aberrant biliary ducts occur normally in some of the lower animals, especially in the fish known as the *Ammocete*, which incidentally is now regarded as merely an embryonic form of the *Petromyzon*. In the lower animals these ducts are known as the Canals of Remak.

The condition of cystic change within ducts that persist in the adult from embryonal rests, has many parallels in pathology; we need mention only thyroglossal, branchial, and urachus cysts; cysts of the broad ligament arising from the parovarian ducts; cysts arising from persistence of Gärtner's ducts; and cysts of the organs of Giralde and Morgagni.

A CASE OF CARCINOMA OF THE APPENDIX COMPLICATED BY PNEUMOCOCCUS PERITONITIS.

E. LIBMAN, M.D.

The object in making this report is to put on record another case of primary carcinoma of the appendix, occurring in a girl, fifteen years of age; to remark upon the complication of pneumococcus peritonitis; and to call attention to the frequency of pneumococcus peritonitis. The patient was a girl, fifteen years old, who entered my service suffering from a chorea of a mild degree, without any organic cardiac lesion. One night

she was suddenly seized with pain in the abdomen, vomiting, and rise of temperature to 102° . The next morning the temperature was 102.6° and there was general abdominal pain and more vomiting. The leucocyte count, which when she was first attacked was 28,000, rose the next morning to 40,000 (polynuclears, 83 per cent). There was general abdominal tenderness and rigidity. By rectum there was a resistance on the right side which was tender. It was suspected that it was a case of gangrene of the appendix or of perforation, as a hyperalgetic cutaneous zone was absent. The girl was operated upon by Dr. Elsberg and on removing the appendix a distinct tumor was found with an elevated edge which was a trifle longer than the tumor seen here. It measured about two cm. in length. The tumor was recognized as a probable carcinoma of the appendix. There were a few ounces of turbid fluid in the peritoneal cavity. In the appendix there was only a slight inflammatory process apart from the new growth. It seemed probable that we were dealing with an unusual process here to account for such a severe blood reaction with such slight acute appendicular change. Specimens of blood were examined fresh. An increase in the fibrin network was found, and it was then thought that there was a strong chance of the condition being a pneumococcus peritonitis. Cultures showed that this was correct. The organism was proven by the presence of the type capsule (Buerger), by the late fermentation of inulin, and by the absence of precipitation of one-half per cent. glucose-serum-agar.

This carcinoma occurred in one of the youngest cases on record; one case was reported at the age of twelve, and two or three at fourteen and fifteen. Attention has been called to the fact that the microscopic

formation of most of these tumors is that described in primary carcinoma of the small intestine (spheroidal celled carcinoma—Rolleston, Brenting). The microscopic examination in this case proved the correctness of the gross diagnosis. The structure of the carcinoma did not conform to the spheroidal celled type.

There are now on record about sixty-five cases of primary carcinoma of the appendix. Rolleston¹ collected sixty-two cases of which forty-two were undoubtedly primary carcinoma of the appendix; Dr. Mandlebaum showed five from Mt. Sinai Hospital last year, three of which had been included in Rolleston's series; and one or two others have been recorded. No recurrence has been reported in any of these cases and the patients have all done well.

As regards the pneumococcus peritonitis, it is valuable to diagnose it before operation. This has been done in two cases reported by Haim² by the high leucocyte count and the increase in fibrin (the counts were not given in the report). Probably numerous cases of pneumococcus peritonitis are never diagnosed. Kelly states that he had not seen a single case of appendicitis due to the pneumococcus. Dudgeon and Sargent³ reported only three cases of pneumococcus peritonitis. In the last few years I have encountered at least three cases of appendicitis with a pure culture of the pneumococcus, eight cases of peritonitis in which the pneumococcus was found in the fluid during life, and six in which it was found post-mortem. Dr. Howard Kelly in his book states that he does not believe that the pure pneumococcus by itself can cause appendicitis. If an organism re-

(1) *Amer. Jour. Med. Sciences.* Vol. CXXXI, 1906, p. 951.

(2) *Wien. klin. Woch.*, 1905, p. 82.

(3) *The Bacteriology of Peritonitis*, London, 1906.

sembling the pneumococcus is found, Dr. Kelly considers it safer to call it a streptococcus. This is an erroneous view. The pneumococcus in peritoneal exudates is apt to take on the morphology of the streptococcus. Dr. Buerger pointed this out in his paper on the staining of capsules. More cases of pneumococcus peritonitis would be discovered if the methods introduced by Dr. Hiss and Dr. Buerger were more widely used.

In cases of chronic parenchymatous nephritis with subcutaneous edema and ascites, pneumococcus peritonitis may come on very insidiously. The cases are apt to go on for several days with general symptoms only (fever, headache, etc.). The fever rises slowly or rapidly after a day or two, and there is a little abdominal tenderness. After a few days have elapsed there is severe diarrhea and then vomiting. There then develops the complete picture of a diffuse peritonitis. If one knows of the occurrence of such a condition, the diagnosis can be made very early. It seems that when ascites is present the pneumococci first grow in the fluid and produce symptoms from the toxin production. When the bacteria have multiplied sufficiently their presence or the change in the fluid (presence of toxin, precipitates and coagula) sets up the peritoneal inflammation.

In corroboration of this view I have found an interesting observation made by Dr. Flexner. He reported in the *Johns Hopkins Hospital Bulletin*, (Vol. VI, 1895, p. 64) in an article entitled "Peritonitis Caused by the Invasion of the Micrococcus Lanceolatus from the Intestine", a case of peritoneal infection by pneumococci in a patient with ascites and dropsy due to chronic parenchymatous nephritis. The diagnosis had not been made before death. Although the fluid was of a milky turbidity, the number of pus cells present was not very large.

Dr. Flexner ascribed the turbidity to the presence of the cocci themselves. I believe we have here an instance of the first step in the production of the lesions in these cases.

In conclusion I want to note that a blood culture made by Dr. Epstein in the case which I have reported, at the time of operation, revealed no pneumococci. This would point against a hematogenous source of the infection.

Discussion.

DR. E. MOSCHCOWITZ thought an interesting point in connection with pneumococcus peritonitis was that if the patient does not die an abscess forms which almost always localizes itself near the umbilicus, and which if allowed to persist ruptures through the latter structure. This feature is so characteristic that a diagnosis of pneumococcus peritonitis can thereby be made.

DR. CHARLES NORRIS asked whether the case had shown at operation an acute or chronic appendicitis, or whether the growth was the only lesion found.

DR. J. H. LARKIN said that he hoped Dr. Libman had not meant to give the Society to understand that all cases of carcinoma of the appendix were complicated with pneumococcus peritonitis. Three of the cases reported by Dr. Kelly had been furnished by Dr. Larkin and knowing the clinical history he was sure that there was no such complication. He thought Dr. Libman should explain more fully the connection which he drew between the new growth and the pneumococcus peritonitis.

DR. LIBMAN said, first, in regard to Dr. Moschcowitz's remarks that the recognized clinical classification of pneumococcus peritonitis was in two types. The first

was the diffuse peritonitis, which acted like that due to other bacteria. In the second type sacculation occurred and there was a tendency to perforate near the umbilicus. As to Dr. Norris' question, Dr. Libman said that the appendix in this case showed slight acute and chronic changes.

DR. LIBMAN said also that in drawing attention to the complicating pneumococcus peritonitis with this carcinoma of the appendix he had done so merely as the consideration of an interesting find and had not meant to establish a connection between them. It was the first case on record in which the combination had been found, but he had not mentioned this in his paper, not wishing to seem to draw a connection between the two conditions. The carcinoma no doubt by obstructing the canal made it easy for an acute appendicitis to be set up by any organism.

A NEW METHOD FOR STAINING POLAR BODIES.¹

A. A. EPSTEIN, M.D.

Dr. A. A. Epstein said that Blumenthal and Lipskerow had made a study of the comparative values of all the different methods devised for staining the polar bodies of diphtheria bacilli and had come to the conclusion that the Ljubinski pyoktanin method gave the best results. But they had found that even with this method difficulty was at times experienced in that it failed to give distinct pictures of the bacillus proper, although the polar bodies might be stained very well. This deficiency

(1) This paper is also published in the *Jour. of Infectious Diseases*, Vol. III, 1906, p. 770.

in the staining of the entire organism constituted an objection to the use of this method, because it rendered the presence of tingibile cocci a possible source of error. Dr. Epstein's own experiences with the various polar body stains compelled him to concur with the view of these authors.

Often a well ripened solution of Loeffler's alkaline methylene blue will define fairly well the morphological characteristics of the diphtheria bacillus. This definition may be greatly enhanced by the subsequent use of Gram's iodine solution as a differentiating agent. Better results can be obtained, however, by the use of a solution of pyronin followed by the iodine solution. The solutions necessary for the purpose are:

1. Loeffler's alkaline methylene blue or a 1 per cent. aqueous solution of pyronin (preferably the latter).

2. Gram's iodine solution.

The steps in the method are as follows:

1. Pyronin solution for 20 seconds, or Loeffler's solution for one-half minute.

2. Rinse in tap water.

3. Gram's iodine solution for 10 seconds.

4. Rinse in tap water, dry, and examine. Counter-stains are not required.

With either of these methods the polar bodies and the body of the bacillus appear very sharply defined, and their relation to each other is very definitely shown. With the pyronin solution the polar bodies appear as large, dark brick red, round or oval bodies, whereas the bacillus is usually slender and of a light red color. In some instances the polar bodies contain an unstained, refractile, central spot.

With the Loeffler solution the polar bodies appear greenish black and the bacillus of a greenish color. In

both instances the entire organism is very distinct, and the contrast between the polar bodies and the bacillus proper is very striking; but the beauty of the pictures which result with the use of pyronin make it a method of choice.

Dr. Epstein showed specimens of diphtheria bacilli in pure and mixed cultures, stained by both methods suggested by him.

BLOOD CULTURES IN TYPHOID FEVER.

A. A. EPSTEIN, M.D.

In the course of some work on the bacteriology of the blood in typhoid fever, extending over a period of a year and a quarter, and comprising a series of eighty-five cases, a feature has been observed in the positive cases which may prove to be of considerable importance.

Cultures were taken as a rule on a number of different media (eight types in all) so as to insure every possible chance for a positive finding. Thus we found typhoid bacilli in the blood of 80 per cent. of our cases. Of the media employed glucose-agar gave the best results, and on it the typhoid bacilli grew in a characteristic manner.

Our observations were made on a 2 per cent. glucose-agar (0.9% acid to phenolphthalein), allowing 0.5 to 2 c.c. of the patient's blood for 15 c.c. of the medium. The mixture was then plated out in Petri dishes. On this medium the bacilli appear normally within the first twenty-four to thirty-six hours of incubation, in very minute, pin point colonies, having a disproportionately wide

area of green coloration around them. This green areola is well defined at the circumference and may be limited by a ring of darkened blood. The colonies show little or no tendency to increase in size for the first two or three days, whereas the surrounding green areola widens very rapidly.

These characteristics apply only to colonies of typhoid bacilli occurring in the depths of the medium. Colonies of this organism appearing at the surface also develop the green color, but they are much larger than the deep colonies of the same age and have nothing that may be considered typical. Such colonies require other means of identification.

In this connection it may be stated that the production of the green color in glucose-blood media is not characteristic for the typhoid bacillus; other bacteria do the same thing. Ruediger studied the question of the production of green color on glucose-blood-agar media experimentally and found that the pneumococcus, *Streptococcus pyogenes*, *Staphylococcus aureus*, and typhoid bacillus produce the green color; whereas *Bacillus coli* does not, producing instead a rapid, diffuse hemolysis. From our own experience, it may be said that the *Staphylococcus aureus* and *Bacillus coli* only need be considered in this connection; the colonies of the other organisms can not be confused with those of the typhoid bacillus. *Staphylococcus aureus* grows in much larger and more disk-like colonies; and, in addition to the green color which it gives rise to, it produces within twenty-four to thirty-six hours an area of clear (complete) hemolysis immediately around the colonies. Outside the area of hemolysis is the area of green coloration. The typhoid bacillus does not do this: the very minute colonies and the very wide areas of green coloration pro-

duced by this organism are so striking that with a little experience one can not fail to recognize them. The colon and the paratyphoid bacilli still require our study.

We have had recently one case of a *Bacillus coli* infection of the blood. In this case the plates of glucose-blood-agar showed much larger colonies than those usually given by the typhoid bacillus. They showed a greater tendency to break through and spread upon the surface, and produced gas within the medium. It is not unlikely that the paratyphoid bacillus will show characters more like those of the colon bacillus, but the actual phenomena which it will give rise to are still to be determined.

The characters which the typhoid bacillus possesses on glucose-blood-agar media affords us a simple and ready means of identifying it early. Most of our positive results were obtained within twenty-four hours after taking the cultures. In some of the cultures, the glucose-blood-agar plates yielded the typhoid colonies after sixteen hours of incubation. In all the cases in which the other media gave a typhoid growth the glucose medium invariably showed the type colonies. In six of the cases the growth on this medium appeared much earlier, and in three cases a positive result was obtained only on this medium.

Dr. Epstein showed plates of glucose-agar with type typhoid colonies in different stages; also plates with the colon bacillus and *Staphylococcus aureus*, and drew attention to the difference between them.

Discussion.

DR. E. LIBMAN referred to a few points about this work. He thought it important because it made the typhoid blood culture method more available for private

practice. There have been introduced recently two methods, those of Conradi and Kayser, the Kayser method being a modification of the Conradi. The blood in these methods is put into a bile medium composed of a mixture of bile and pepton for sixteen hours. Plates are made on the Conradi-Drigalski medium. With this method an expert can easily state he has the typhoid bacillus or an organism in the typhoid-colon group as soon as he finds a Gram negative bacillus, but people who are not so expert can not be sure of not having contaminations. Dr. Libman had seen organisms which he was sure could easily have been placed in the typhoid group unless a careful study of them were made. On going over a good deal of the work which has been done and noting what the observers had done to verify their organisms, it was found that proper steps had often not been taken. This find of Dr. Epstein's had been a great surprise to Dr. Libman. It had been their custom in the laboratory for several years to use a number of media in this work. No particular attention had been given to studies on typhoid. He had come to the conclusion that glucose-agar had no particular advantage in blood work, except as a control for glucose-serum-agar. He was therefore surprised to learn that on this medium the typhoid bacillus gives a distinct colony. He thought it would be wise to study a number of blood cultures before basing reports on the method. After seeing the colonies a few times one could not make a mistake except perhaps as regards paratyphoid. As to the question of titer, Dr. Epstein had found that 0.9 per cent. acid was the most favorable. Agar media made up in the usual way ends ordinarily at about 0.9 per cent. acid. The main point is the fact that with this method no dilution of the blood is needed. The only other observer

who has had good results with concentrated blood is Schottmüller. Dr. Libman said that in the future it was their intention to combine this method of Dr. Epstein's with those of Conradi and Kayser in the laboratory. Recent studies show that Dr. Epstein's method gives more results than the bile method.

DR. WARREN COLEMAN said that he had been very much interested in this report, especially as he and Dr. Buxton had been working along similar lines. What had surprised him most was that Dr. Epstein had got his cultures with undiluted blood. There had been a general belief that coagulation of the blood caused destruction of the typhoid bacilli. They had therefore been working with high dilutions. This summer they had adopted the bile medium of Conradi which contains, in addition to bile and peptone, 10 per cent. of glycerine put in with the object of preventing the development of saprophytic organisms which commonly enter as contaminations. They had been most successful with this medium. About forty cases had been examined and a positive result had been obtained in every one. There was only one case in which they had failed to get a positive result the first time, and that was towards the end of the disease when the temperature was nearly normal. Dr. Buxton had sent his reports to the hospital as a rule within twenty-four hours. The procedure is as follows: Usually 10 c.c. of blood is taken from a vein at the bend of the elbow, This is immediately divided among several flasks of the bile medium in the proportion of 1 part of blood to 3 of the medium. The flasks are then put in the incubator over night, the specimens usually having been taken in the afternoon. The next morning streaks are made on litmus-lactose-agar plates. By afternoon

they show a growth, if bacilli are present. If the organisms possess the morphological characteristics of the typhoid bacillus and the surrounding medium is not reddened, Dr. Buxton is certain that he is dealing with this bacillus. Positive identification is made later with immune serum. Personally Dr. Coleman did not consider the method practical in its present status. It is a difficult thing to get the blood in a private house, although it is routine in hospitals. It is hard to overcome the objections of the patients and most private patients would be frightened by the necessary preparations. He felt that the method would not become practical until it was brought to a basis where the test could be made with the amount of blood which can be drawn from the finger or ear.

DR. F. C. WOOD asked Dr. Epstein how early he was able to get his cultures; that is at what period in the disease the organism could be demonstrated in the blood with such constancy as to be an aid to diagnosis.

DR. EPSTEIN said that most of his positive results were in the second week. That only 80 per cent. of the cases yielded positive cultures he attributed to the fact that these cultures were taken indiscriminately and very often towards the end of the disease. Had the cases been chosen, the results would undoubtedly have been better. Dr. Epstein's experience with the bile medium of Conradi was limited, but so far the glucose-agar medium had given better results. As regards the identification of the organism, he suggested that this method be used for early tentative diagnosis. The final proof of the absolute identity of the organism must rest with cultural and agglutination methods. Dr. Epstein identified his organisms finally both by culture and by agglutination with standardized typhoid immune sera.

DR. E. LIBMAN said that in looking over the records he had found that in the cases which could be proven to be in the second week the results were 100 per cent. A large number of late cases had been examined. Another point was that at his request Dr. Epstein had used six agar media of different composition and the flasks, so that of the entire 15 c.c. of blood taken only 1.5 c.c. could be used in this medium. In the future he thought they would use nearly all the blood on glucose-agar so that the results might be expected to be much higher.

DR. EPSTEIN said as regarded the concentration of the blood, that he rarely used more than 2 c.c. to the 15 c.c. of medium. If more is used the area of green color about the colonies is not as distinct nor as wide. The less blood present the wider the area of green coloration. Ruediger suggested that this color is due to the development of biliverdin caused by the production of lactic acid resulting from the fermentation of the glucose.

A STANDARD BLOOD MEDIUM FOR BACTERIOLOGICAL WORK.

E. P. BERNSTEIN, M.D., AND A. A. EPSTEIN, M.D.

Dr. E. P. Bernstein, in presenting a new method for sterilizing blood for cultural purposes, said that though great attention has been given of late to blood media, the necessity for a method which would make such media more widely applicable has been felt. Much of the difficulty hitherto experienced has been in obtaining sterile blood readily and in quantities sufficient for

universal use. This difficulty compelled various investigators to select widely different animals for their source of supply, some even resorting to the use of commercial hemoglobin. The work therefore was varied, and no standard blood media could be established.

After a series of experiments Dr. Bernstein and Dr. Epstein had been able to devise a method by which the difficulties previously mentioned may be overcome. Numerous attempts have been made in the past to sterilize the blood to be used for cultural purposes, but of the methods so far introduced there is none which permits of sterilization without at the same time altering the character of the blood. For the purpose of obtaining unchanged blood upon which the (so called) hemolytic and other effects of bacterial growth could be determined, they resorted to the use of formalin as a sterilizing agent. It was found that formalin could be used for this purpose without later exhibiting any inhibitory influence on the growth of bacteria. In order to prevent clotting of the blood, ammonium oxalate was employed. The ease with which beef blood can be obtained in large quantities in any abattoir led to the selection of this source of supply.

As a result of their experiments the following method was presented as being the most satisfactory: Four hundred c.c. of beef blood are drawn directly into a sterile Erlenmeyer flask of 500 c.c. capacity containing 30 c.c. of a one per cent. solution of ammonium oxalate (in distilled water) and 0.5 c.c. of formalin of 40 volume strength. The flask is then shaken for one or two minutes. Thirty minutes is required for the sterilization, so that by the time the flask reaches the laboratory the blood is already sterile. The blood is then transferred in small quantities into sterile Erlenmeyer flasks and di-

luted with twice its volume of one per cent. saline solution. This dilution reduces the actual formalin content to 1 part in 2,400 of blood. According to their experience it was best to allow this diluted blood to stand for 24 to 48 hours at room temperature before employing it for cultural purposes so as to permit better diffusion of the formalin. The blood at this stage must receive the same care as any other sterile nutrient medium. The flasks are then sealed and stored on ice until needed.

In the preparation of the media Dr. Bernstein used the diluted blood in the proportion of 1 part to 15 of nutrient material (agar or broth). This quantity of blood had been found to be the optimum for showing the character of growth, color changes, and hemolysis. The final product has an absolute formalin content of 1 part in 36,000. The ordinary laboratory organisms are found to grow very well on these media and luxuriant growths of pneumococcus, meningococcus, gonococcus, and influenza bacillus are readily obtained. Full details of various observations will appear in a later publication.

Throughout the entire procedure of sterilizing the blood, there are no evidences of any gross or microscopical changes. The blood remains of the same scarlet color as when first drawn and the blood corpuscles are unaltered. This permits of the separation of the blood corpuscles from the serum, if so desired. This may be accomplished by centrifugalization or by allowing the blood to stand and then washing the sedimented corpuscles in several changes of sterile salt solution. No doubt media prepared with washed corpuscles and those prepared with entire blood would be found to give interesting cultural differences. In the use of the former any possible bactericidal effect of the serum would be eliminated.

It was stated in this connection that an occasional beef would yield blood of a deep crimson color. Such blood should not be selected for the work as laking has occurred, which naturally interferes with the study of hemolysis. In time (10 to 12 weeks) the stored blood begins to assume a darker color and is then also useless for observing the finer hemolytic changes. Its usefulness for cultural purposes, however, remains unimpaired. Blood agar plates in which the blood was five months old were exhibited and showed luxuriant growths of influenza bacillus, pneumococcus, *Streptococcus pyogenes*, *Streptococcus mucosus*, meningococcus, gonococcus, *Micrococcus catarrhalis*, *Staphylococcus albus*, *Staphylococcus aureus*, and typhoid and colon bacilli. Blood agar plates in which the blood was five days old also showed luxuriant growths of these organisms, besides demonstrating their various hemolytic powers and chromogenic changes.

From this work there had branched out numerous possibilities, one of which had been followed up in an experimental way though it was still in embryo. Two organisms, the typhoid and colon bacillus, had been dealt with on media consisting of agar containing 1 per cent. of the various sugars, to each 15 c.c. of which about 1 c.c. of five months old blood had been added. In all sixteen different sugars were tested, and very interesting results had been obtained by surface inoculations.

On lactose-blood-agar the typhoid bacillus failed to hemolyze the medium, whereas the colon bacillus produced distinct hemolytic changes. On raffinose-blood-agar the morphology of the colonies was distinctly different, the typhoid colonies appearing umbilicated with radiating striae, while the colon colonies failed to show these peculiarities. Ordinary blood-agar also showed these differences in morphology, but to a somewhat less

degree. Maltose-blood-agar caused the typhoid colonies to assume a deeply pigmented, almost black, appearance; the colon colonies retained their dull white color. Dextrose-blood-agar gave the most marked differences, the typhoid bacillus causing precipitation of the medium, showing no hemolysis, and giving the almost black appearance to the colonies; while the colon bacillus failed to precipitate the medium, showed distinct hemolysis, and left the colonies unpigmented. On 5 per cent. glycerine-blood-agar the same differences of pigmentation as observed on maltose-blood-agar were seen, but to a more marked degree.

The late appearance (three to five days) of the above difference on all the media used lessens the practical application of these facts, but with further experimentation they may be made available for an early diagnosis.

Discussion.

DR. A. A. EPSTEIN thought it might be in place to say a few words with regard to the reason certain steps were gone through in the preparation of this blood. After sterilizing the blood with the formalin it might seem more logical that a certain quantity of the whole blood should be used in a given proportion to the medium, instead of first diluting the blood and using a larger volume of the diluted blood. They had used 1 part of diluted blood in 15 parts of nutrient medium, the ultimate result being the same as using 0.3 c.c. of the whole blood to 15 c.c. of the medium. They had found by experiment that the growth obtained in mixtures with undiluted blood, however, were not as rich as those obtained with the diluted blood. This was possibly due to the greater diffusion of the formalin which took place on

diluting the blood. The chemical changes had not been gone into. The morphology of the old blood was not much altered because the formalin acts as a preservative of the individual cells. The physiological changes which took place in the blood Dr. Epstein knew nothing about, but hoped to study them, especially the physiological changes which take place in the leucocytes immediately on adding the formalin to the blood. The subject would be approached in two ways: first, by testing whether the cells retain their phagocytic properties; and secondly, by testing whether the blood withdrawn from an animal would, after being sterilized, act injuriously when introduced into the same animal.

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DR. F. S. MANDLEBAUM, *President.*

MICROSCOPIC PREPARATIONS OF SOME RENAL AND ADRENAL MALFORMATIONS.¹

EDWIN BEER, M.D.

Dr. Edwin Beer showed under the microscope five specimens of interesting findings in kidney and adrenal anatomy, three being slides of cystic kidneys, and two slides of adrenal rests in the liver and kidney. As regarded the cystic kidneys, Dr. Beer said that these were congenitally cystic, the children having died a day or so after birth. It was interesting to note the various explanations which had been given of these cystic kidneys, one, suggested by Virchow, being that they were caused

(1) A report of these cases of adrenal rests in the liver has been published in the *Zeitschrift f. Heilkunde*, Bd. XXV, 1904.

by the dilatation of the tubules and Malpighian bodies as the result of obstruction. It was now known that obstruction of ducts does not lead to cystic dilatation but to atrophy of glandular organs, as has been shown by experimental work. Chief among the later theories was that of Van Kahlden and Hufschmidt, etc., that the tumors were real neoplasms. At the last German Congress it was evident that Van Kahlden had been misled by several pictures in cystic kidneys, from which he had surmised that the whole condition was a neoplasm. Marchand summed up the criticism of this view in these words: "The whole theory of neoplastic origin does not apply; it has no basis." About midway between these theories was the suggestion which had been made that there was probably an embryological fault; that the glomerular end did not unite with the end near the pelvis, and that owing to the failure to unite these cysts resulted. This theory did not gain particular support, until Ribbert in going over the question came to the opinion that the uriniferous tubules developed from one anlage and the Malpighian cysts, from another. He also showed that these kidneys have two types of cysts, a tubular cyst and a Malpighian body cyst. In the tubular cyst one finds the common tubular epithelium lining the membrane. For a time it looked as though Ribbert's theory would not hold, as work was produced tending to show that the uriniferous tubules and the Malpighian bodies develop from one anlage. Further studies, however, have shown that Ribbert was correct; and that the tubules arise from one anlage and the Malpighian body from another. It was interesting to note that these types of cysts are associated with other congenital malformations. This had been shown to the Society lately by the demonstrations of

Drs. Weil and Moschcowitz. Dr. Beer had under the microscope an excellent illustration that these kidney cysts were malformations. This specimen was of a congenital cystic kidney showing two glomeruli growing in one cyst. Specimens of congenitally cystic kidneys with only tubular cysts and others with Malpighian and tubular cysts were also shown under the microscope.

As regarded the adrenal rests, Dr. Beer said that these were very common. In a large series of autopsies adrenal rests were found in the kidney and along the vessels all the way down to the ovary in the female and to the testicle in the male (in 90 per cent.) Up to a few years ago it had not been realized that these rests did occur in the liver. There were only five cases of adrenal rests reported in the liver. Dr. Beer had specimens from six cases in which he had discovered them situated in the capsule of the liver. A peculiar point which must arise is this: why, when these adrenal rests were found in one hundred and fifty cases in the liver, do not neoplasms such as hypernephromata develop in the liver as frequently as they do in the kidney. Hypernephromata in the liver are most rare; the literature contains only two cases, one of which is doubtful. Another interesting fact shown by the specimens under the microscope was that adrenal rests are not always encapsulated. Hypernephromata, however, until they break through their capsules usually are encapsulated. In the specimens under the microscope one could not see any demarcation between adrenal and kidney cells. Moreover, in the center of the "rest" there were distinct kidney tubules.

In closing, Dr. Beer reminded the Society of Croftan's publication of a biological test of hypernephromata, based on the facts demonstrated in connection with "adrenal diabetes."

Discussion:

Dr. JAMES EWING asked Dr. Beer whether any of the authors to whose studies he had referred gave a satisfactory explanation of the mechanism of the development of these cysts. It seemed clear that they were tubules and capsules of the glomeruli; but why did they dilate?

Dr. BEER said there was no doubt that Dr. Ewing's question was very apropos. It applied to all cysts as well as to these kidney cysts. Why do they dilate? He could only say that, as far as analogy went, in the study of other kidneys cysts he had found something which he had not as yet found in these congenital cysts, which might explain the dilatation; namely, a marked change in the epithelium in the kidney. As a result of the change there was an exudation of colloidal material which distended the cysts. In these congenital kidneys there was a very small amount of colloid, and perhaps the same process took place in them.

A CASE RESEMBLING PSEUDOLEUKEMIA
IN A CANARY. A CASE OF ARTERIO-
SCLEROSIS WITH PRODUCTION OF BONE
AND BONE MARROW IN THE AORTA
OF A COCKATOO.

G. R. SATTERLEE, M. D.

Dr. G. R. Satterlee presented two cases of birds on which he had performed autopsies. Although this might seem to be entering on comparative pathology, the conditions were similar to those found in man, and therefore of interest.

In the case of the canary very little history was obtainable. The bird had had diarrhea and wasting for some time with loss of appetite. Fullness in the abdomen was also noticed. The bird was two years old. Post-mortem the body was very much emaciated and in the abdomen a large mass was felt in the region of the spleen. This was about 3 by 0.5 cm. in size. The tumor was freely movable and attached by a small pedicle. It was firm on section, round, and non-lobulated. The liver was large and had yellowish nodules on the surface, making it extremely irregular in shape. The kidneys were mottled, of a greenish-yellow color, and the remaining tissue was normal. The lymph glands were not enlarged. No blood count was made during life. Microscopical examination of the splenic tumor showed a very thick, fibrous capsule, containing numerous large and small blood vessels, thick septa with veins, and Malpighian corpuscles, so that it was undoubtedly the spleen. The mass was made up of circumscribed and diffuse collections of small mononuclear cells. It also had some large mononuclear cells and a few polynuclears and eosinophiles. The nuclei of these cells were nearly all of the pyknotic type and a great many were fragmented. No typical mitotic figures were seen. The cells of the Malpighian corpuscles showed a marked degree of karyorrhexis. There was no necrotic tissue in the spleen. There was no gross evidence of tuberculosis. Examination for tubercle bacilli was negative. Examination of the blood in the splenic arteries showed apparently no lymphocytosis. In the stroma of this tumor there was a large amount of fibrous tissue as bands and scattered around generally. In places the leucocytes were breaking out into the capsule and into the blood vessels. From microscopical examination it was concluded that the growth was a lymph-

oid hyperplasia which originated probably in the Malpighian corpuscles. There was also interstitial splenitis.

In the liver there was a collection of cells of very similar character to those in the spleen, partly surrounded by fibrous tissue and partly extending into the liver tissue itself. The liver cells showed fatty degeneration and general breaking down. No mitotic figures could be demonstrated. In some of these circumscribed masses there were a number of new blood vessels, showing the possibility of a malignant growth. The rest of the organ showed an extreme amount of interstitial cirrhosis with large bands extending throughout the liver tissue, somewhat similar to the bands found in a syphilitic cirrhosis. Another interesting point was the increase in the smaller bile ducts, a sort of adenoma of the bile ducts, analogous to a biliary cirrhosis in man. The lungs were normal; there was no evidence of tuberculosis. Examination of the blood in these vessels showed no lymphocytosis.

The kidney showed fatty degeneration of the convoluted tubules; the glomeruli were shrunken. The capsule of Bowman was thickened; the subcapsular spaces contained casts. The lesion in the kidney was a parenchymatous and glomerular nephritis. Close to the kidney there was a small glandular structure in which was an evident metastasis. The remaining tissue showed no change, except in the heart where there was a small collection of lymphocytes in a lymphatic space. This case might be considered either as a hyperplasia of the lymphatic tissue of a non-malignant nature, or as a new growth. General leukemia was ruled out by the blood examination. Dr. Satterlee gave a review of the literature of cases of leukemia and pseudoleukemia.

The second case was a white cockatoo which had very little history except that of neglect. Autopsy

showed extreme atheroma of the whole aorta. Dr. Satterlee said that he had autopsied about 100 birds and had never seen a case of atheroma, except for a few patches in the arch of the aorta in one bird, which was the reason why this case was especially interesting. The atheroma extended down the whole length of the aorta through the thoracic and abdominal aorta. The cervical branches of the aorta showed apparently an obliterating endarteritis. There was atheroma around the auricular valve and around the coronary artery. There was a general arteriosclerosis of all the vessels in the body. There were arterial changes in every organ except the spleen, in the majority of cases in the media, but also in the intima. The vessel walls were edematous and the muscle cells separated. In the aorta the whole of the media was occupied by this apparent bone formation. It was said that cartilaginous formations in the aorta of the bird are not uncommon. In this case outside of the bone there were two cartilaginous plates. Inside of the bone there was true bone marrow. The intima was very irregular in this aorta and dipped down in places until it met the cartilage and bone. Marrow cells were present, but no giant cells. Polynuclear leucocytes and a few red blood cells were found. Bone absorption as well as bone formation was going on, as evidenced by some typical Howship's lacunæ.

There is but little literature on this subject. Bunting has reported a case of the formation of true bone in a sclerotic aorta. The principal changes in his case were in the media. He attributes this process of bone formation to some injury or to decomposition of calcium salts giving rise to hyperplasia of connective tissue. In Dr. Satterlee's case the calcium salts were deposited not only in the cartilage but also in the tissue of the media.

A summary of all cases investigated by Bunting shows that he found bone in the aorta six times, in the medium sized arteries twenty-two times, and in the heart eight times. Experimental bone formation with calcium salts has been accomplished by injection of incinerated bone into the peritoneal cavity of cats, and by tying off the renal artery in rabbits.

Discussion.

DR. F. C. WOOD said that Drs. Williams and Busch had reported on lymphomatous tumors of the dog's spleen, in the *Journal of Medical Research*, Vol. VII, 1902, p. 408. Their results showed that tumor-like nodules were present in two and one-third per cent. of seven hundred and twenty dogs examined. Lately there had been more reports in the journals of leukemic and pseudoleukemic disease in animals, lymphatic and myelogenous leukemia being described, so that such conditions were evidently not at all uncommon. Dr. Wood asked whether the cockatoo had shown any symptoms of gout or not. Gout was very easily produced in chickens by the administration of toxic substances which injured the kidneys.

DR. SATTERLEE said that there was no history of the bird. There were no gouty deposits. A great many birds with gouty deposits had no arteriosclerosis.

MISS POPE said that the family owning the bird had been abroad, and the bird having been left to the care of servants showed signs of great neglect. It was really in a very bad condition.

A CASE OF PHOSPHORUS POISONING IN A CHIMPANZEE.

ISRAEL STRAUSS, M.D.

Dr. Israel Strauss presented specimens from a case of phosphorus poisoning in a chimpanzee, saying that though examples of phosphorus poisoning were not uncommon in the human subject or in animals, yet since the cost of a chimpanzee precluded its use for experimental purposes, this case was interesting because of its rarity. The chimpanzee was one of two recently brought to this country from Africa and placed in the American Museum of Natural History. Shortly after its arrival it was taken ill and lost flesh rapidly; its hair fell out and its appetite became poor and it coughed. As these animals die general of tuberculosis it was thought that this one might be tuberculous, and the Director of the Museum ordered its removal. Before it could be removed, however, it died. The lungs at autopsy showed no evidence of tuberculosis. They were very pale. There was no pneumonia. On the visceral pleura there were a number of ecchymoses about the size of a pin head. The parietal pleura had no ecchymoses. The mesenteric glands were enlarged, pale pink in color, and showed no signs of tuberculosis. The intestinal mucosa appeared somewhat congested and slightly thickened. The spleen was slightly enlarged; the glomeruli prominent. The kidneys had the appearance of advanced degeneration. The liver was enlarged and appeared very fatty, most of it being yellow, some areas red, and the lobules rather indistinct. The autopsy, of course, determined that there was no tuberculosis, and it appeared that the animal has suffered from some toxemia, suggesting either arsenic or phosphorus poisoning. It was learned that it

was customary to feed chimpanzees calomel very freely, but the symptoms did not point to mercurial poisoning. The owner later accounted for the condition by saying that on the voyage from Africa the sailors amused themselves by feeding the chimpanzee on matches. The microscopical examination bore out the assumption that the animal had died from phosphorus poisoning. While the macroscopical examination showed only marked degeneration the microscopical showed the center of the lobules necrotic with disintegration of the cells, some showing marked fatty degeneration, others having entirely necrosed. There was marked congestion in the center of the lobules and in some cases hemorrhage. It was striking to compare the picture of this liver with the liver of a patient who had died from toxemia of pregnancy. In this latter there was the same appearance, the middle zone being the one which had necrosed in both instances. Paltauf, in 1902, made the statement that in acute yellow atrophy necrosis generally began in the central zone, while in phosphorus poisoning it began in the peripheral zone. In this animal the opposite was the case, and Dr. Strauss doubted whether Paltauf's statement would hold even with the human subject.

MULTIPLE SYSTEMIC SARCOMA OF MYELOGENOUS ORIGIN.

CHARLES NORRIS, M.D.

The case I am about to present was that of a patient in the wards of Bellevue Hospital, in the service of Dr. Egbert Le Fevre. I am greatly indebted to Dr. Le

Fevre for permission to present at this time an abstract of the clinical history. The case will be reported in full later, with Dr. Le Fevre.

The patient was a boy, sixteen years of age, a piano player, of good habits, with no history of previous illness or of venereal disease. The family history was likewise good.

The patient had been losing weight for an indefinite time. Six weeks previous to admission, May 3, 1906, he noticed a few nodular swellings behind the angle of the jaw, and also that he was gradually becoming weaker. Later, he became aware of a mass in the left side of the abdomen as well as of nodules about the size of a pea in the abdominal wall, which were movable and not tender. No other symptoms, except daily increasing weakness, were elicited. His appetite was good. A week before admission he complained of pain in the left hip, which radiated down the thigh. Since then the pain had been continuous in the left knee and hip, without any swelling of the joints.

On admission his temperature was 101.4°; pulse, 120; respiration 20. Patient was a boy of small frame, and poorly nourished. The skin was pale; the mucous membranes anemic. There was a small discharging pustule over the left buttock. The lymph nodes in the neck were greatly enlarged. All the superficial lymph nodes were easily palpable and firm. In the subcutaneous tissues of the neck there were found a few large masses which were irregularly nodular, movable, and not attached to the skin. Numerous small nodules were felt through the skin of both upper arms, and in the epigastrium. Above Poupart's ligament on the left side was felt a firm mass about the size of a hen's egg, which was not attached to the abdominal wall. The rounded border of

the liver was felt indistinctly about one inch, the spleen about three inches, below the costal arch.

On May 7, four days after admission, one of the subcutaneous nodules was removed and examined outside the laboratory, and I am informed that the diagnosis of alveolar sarcoma was made.

Two weeks after admission the patient complained of pain and tenderness and pressure in the left axilla, and a few friction rales were heard.

On May 18, the next day, another small subcutaneous nodules was removed and examined by us.

The patient died suddenly on May 19, sixteen days after admission.

The urine was examined twice, and was found negative. There is no record of the presence of the Bence Jones albumin in the urine, the test probably not having been made.

Two examinations of the blood were made. The first day after admission the red blood cells were 3,940,000; white cells, 8,600; hemoglobin, 55 per cent. The red blood cells showed poikilocytosis and central pallor. A few normoblasts were present. Two weeks later, three days before death, the red blood cells were 2,800,000; white cells, 8,600; hemoglobin, 45 per cent.

One blood culture, made eight days before death, was negative. The patient ran a daily evening temperature of 100°. The last two nights it ran to 101°.

After considerable difficulty, consent for an autopsy was obtained and this was performed fifty hours after death. Only a brief abstract of the autopsy findings need now be given.

The various organs showed a slight degree of post-mortem change. The body was that of a boy of medium stature, markedly emaciated. Numerous shot-like nod-

ules were felt in the subcutaneous tissue of the neck and thorax, and there were a few on the back, abdomen and upper extremities, none being present in the lower extremities. The lymph nodes in the axillary and inguinal regions were not enlarged.

The peritoneal cavity contained about three liters of serofibrinous fluid. The omentum presented a very striking picture, appearing as a large apron covering the intestines. In places it was at least two cm. in thickness. The spleen extended below the umbilicus; the liver several inches below the free margin of the ribs. On the removal of the sternum and cartilages, which were normal in appearance, a series of small, firm nodules, two to three mm. in diameter, were found, adherent to their inner surfaces. All the cervical lymph nodes, the superficial as well as the deep chains of nodes, were enormously enlarged, forming large, more or less adherent packets on either side of the trachea and thyroid. In general, the individual nodes were discrete, but were firmly matted together with adhesions. In places the outlines of the individual lymph nodes were not sharply delineated, the nodes being more or less intimately fused together. The largest nodes were situated along the carotids, just above the bifurcation, and measured roughly 5x3x2 cm. The smallest nodes were whitish gray and, on section, homogeneous, permitting no juice to be scraped off. The larger nodes showed central yellowish areas of necrosis, some of which were softened. In other places there were irregularly shaped areas of hemorrhage and hemorrhagic softening.

The thyroid gland preserved its normal contour, measuring 6 cm. in breadth. Many whitish nodules and in places, larger masses were present throughout the gland. Only a small portion of normal tissue was ap-

parent. In the region of the thymus there was a large mass of tissue measuring 10x8x4 cm., extending over the pericardium. It was composed of a series of larger and smaller nodules. No thymus-like tissue was discernable on section.

The pleural cavities contained about a liter of sero-fibrinous fluid. The costal and diaphragmatic pleurae were studded with numerous elevated, whitish, firm nodules varying in size from a pinhead to the size of a large pencil, and hard, flattened, but elevated plaques. The visceral pleurae were likewise studded with nodules, some of which were flat and sessile, others more or less pedunculated. No nodules were present in the lung tissue proper, or in the bronchial nodes, both of which were free from tuberculosis. The tracheal nodes, however, presented large tumor masses.

Heart. The mediastinal surface of the pericardium presented a series of nodules resembling strings of smaller and larger pearls. A few raised nodular foci were found upon the coronary veins. The interauricular septum was thickened with tumor tissue, and minute nodules were present in the papillary muscles of the left ventricle.

Liver. The liver weighed 2,090 grams. It was thickly studded with tumor masses varying considerably in size, shape, and general appearance. In general, they were sharply circumscribed, some of the nodules being surrounded by a translucent fibrous capsule.

Spleen. The spleen was very large, weighing 1,080 grams, and measuring 21x16x9 cm. Like the liver, it was the seat of extensive tumor infiltration.

Adrenals. The adrenals weighed 55 grams together. They were studded with tumor nodules, little normal tissue being present.

Kidneys. The kidneys together weighed 350 grams. The capsules on their external surfaces were found studded with large, confluent nodules, also flat foci, 1 to 2 mm. in size, and raised nodules of intense purple color, 3 to 4 mm. in diameter.

The left testicle was situated within the peritoneal cavity in a mass of enlarged lymph nodes. The organ was infiltrated with hemorrhagic and softened tumor tissue.

The periportal lymph nodes were greatly enlarged. The peripancreatic lymph nodes were infiltrated. The pancreas presented a few small tumor nodules.

The entire alimentary canal, from the mouth to the anus, especially with regard to the mucous membrane, was normal. Along the mesenteric attachment of the small and large intestines were found innumerable smaller and larger spherical nodules, varying greatly in size, the largest being about the size of a large lime. Similar nodules and plaques were scattered along the serosa of the mesentery. The mesenteric and retroperitoneal lymph nodes were all greatly enlarged. As in the case of the cervical lymph nodes, these nodes, although adherent, retained their normal shape, and in only a few places had the individual nodes become confluent.

Head. The pericranial tissues, especially on the right side, were thickened, large, flat masses of tumor-like infiltration being present over the convexity. The parietal bone over the boss was eaten away or depressed. There was a distinct softening of the bones of the calvarium in their entirety, especially on the right side, on account of infiltration with tumor tissue. The dura mater was quite adherent, and was the seat of extensive tumor thickening, which, over the right frontal region, had caused a marked depression in the region of the 2d

and 3d frontal convolutions. The brain, the pituitary and pineal glands, the ears and sinuses, were normal.

The marrow of one of the lumbar vertebræ which was examined was pale, but presented larger and smaller areas which were soft and somewhat reddish in color. The lower diaphysis and the lower portion of the shaft of the right femur were hyperemic, the marrow being grumous. There were also a few small areas, about 3 mm. in length and breadth, which were whitish in color, and somewhat firm. The marrow of the ribs appeared very scanty, the bone having a hollowed out appearance.

The case briefly reviewed exhibits many noteworthy features. Perhaps the first in importance is the extensive distribution and abundance of the tumor-like foci; secondly, the noteworthy involvement of widely scattered tissues which, however, are closely related functionally; namely, the diffuse involvement of the marrow of one of the long bones, the vertebra and the calvarium, the extensive nodular infiltration of the serous surfaces of the pleura, peritoneum, and dura mater, and of the omentum, the lymph vessels of the mesentery, and the liver and spleen. The hematopoietic systems, marrow, liver and spleen, were accordingly extensively involved. In association with these lesions, the mediastinal, cervical, peripancreatic, portal, mesenteric and retroperitoneal lymph nodes were likewise extensively infiltrated. On the other hand, the organs not related to the lymphatic system, at least in the functional sense, such as the brain and lungs, were practically uninvolved.

It will occur to all that this case presents an analogy, at least anatomically, to the picture presented by leukemia and pseudoleukemia. The absence of metastases in the lungs and brain, the comparatively slight involvement of the other organs, with the exception

of the suprarenals, and the extensive involvement of such widely separated but functionally closely related organs is at least very striking.

The malignancy of the tumor, judged by its tendency to invade the surrounding tissues, as in the lymph nodes, is not marked. Thus, only in a few places have the individual lymph nodes forming the large masses of glands, become confluent. In other words, the growth in the lymph nodes shows no marked tendency to break through its capsules. This, however, has occurred by local invasion from the iliac nodes into the testicle and retroperitoneal nodes.

The histology of the tumor nodules, which is essentially the same throughout the various tissues, may be described briefly. The changes found in these bones, on account of their great interest and importance in connection with the case, may be described first.

The marrow of the femur presents a remarkably homogeneous appearance. The smaller and larger spaces between the bony lamellæ are filled with large spheroidal cells, which are markedly uniform in appearance. The picture presented is thus totally unlike that of normal red bone marrow. The cells are large and, when free, distinctly spheroidal in shape. The protoplasm is markedly eosinophilic and, except with the high power is homogeneous. The nuclei are large and round, usually distinctly vesicular, showing a more or less marked chromatin network, and one or more nucleoli. In the smaller cells the nuclei tend to stain more deeply and uniformly. A delicate stroma with rather wide meshes is occasionally made out, especially in the sections of the calvarium.

The cells greatly exceed in size the plasma cells. They possess no specific granulations characteristic of the myelocytes. These cells resemble strikingly those

depicted by MacCallum, and possibly those shown by Quackenbos, in their cases of multiple myeloma. The sections of the calvarium and the body of one of the lumbar vertebræ present a similar histological picture to that of the femur. With MacCallum we may consider the cells as directly related to the myelocytes, and probably derived from, or similar to, the large non-granular forerunners of these cells.

The tumor nodules found elsewhere in the body show a striking similarity in their histological picture, especially in reference to the cells which we have described as replacing the normal cells of the marrow. They are more or less spheroidal in shape, and only when the cells are closely aggregated do they tend to become polygonal. The nucleus is usually central, and is relatively large, but occasionally it is eccentric as in the plasma cells. The chromatin content varies greatly, some of the nuclei staining intensely and diffusely, but usually the chromatin is scattered throughout the nucleus in the form of rods and strands, or forms a more or less definite network. The majority of the nuclei have distinct nucleoli which are large and take an intense red color with the methylgreen-pyronin stain. There is a distinct nuclear membrane. Numerous mitotic and karyolytic figures, and irregular divisional forms are seen, which may be held to be an evidence of the rapid proliferation of the tumor cells. The cytoplasm stains rather intensely with eosin, and appears somewhat stippled or granular, and with methylgreen-pyronin stain has an intense reddish color. No granulations of any variety could be detected in sections stained with Giemsa or Unna's polychrome. Many of the nodules are surrounded by well defined connective tissue capsules, from which are given off delicate septa which form a supporting reticulum for the tumor cells.

No fibrin could be demonstrated between the cells with Weigert's stain.

In many places no connective tissue stroma is made out, and the cells are separated merely by a granular intracellular substance in which are nuclear fragments and red blood cells. The reticulum does not, therefore, appear to be a constant or predominating feature of the structure. The vascularity of the tumor tissue varies greatly, but nowhere is the presence of new formed blood vessels a striking feature. Areas of hemorrhage and necrosis are frequently encountered.

We wish to call your special attention to the peculiar and highly colored small nodules in the liver and spleen, which have imparted such a brilliant appearance to the slices of these organs. The color is a deep purple. The Kaiserling preparations here shown have practically preserved the color, although the tint is paler than in the original specimen. The largest of these nodules does not exceed 5 mm. in diameter. Sections of these nodules show the same tumor cells in abundance, mixed, however, with numerous red blood cells, with a fair number of nucleated red blood cells, resembling normoblasts. These nodules we consider approach closely the type of tumor which Ribbert describes as erythroblastoma. It is known that under certain pathological conditions, as in syphilis (Askanazy), the blood forming function of the liver may reappear in extrauterine life.

We have thus in our case a tumor-like process in which large and non-granular cells and erythroblastic cells are present. The presence of these nucleated blood cells or normoblasts may possibly be accounted for upon the basis that the tumor cells being the original and undifferentiated elements of the bone marrow or "Stammzellen" have developed into erythroblasts, a view which has been expressed by Scheele and Herxheimer.

The presence of red blood cells in a well preserved condition in small groups and in close association with the tumor cells is certainly striking. There is no evidence of the breaking down of the red corpuscles, and no hematin crystals are present, which one would expect if an actual hemorrhage had occurred.

So much at this time for the essential structural features of the tumor. It was in the bone marrow from the femur and the vertebræ that the most complete replacement of normal tissue by the characteristic tumor cells was encountered, and in the sections under the microscope we can see that the spaces between the trabeculæ are entirely filled with large round cells, such as compose the tumor masses elsewhere. It is this extreme involvement of the bone marrow, such as is found in all the leukemias and the various types of myelomas, that has inclined us to the belief of the myelogenous origin of the tumor-like process.

The case before us exhibits in the present state of our knowledge, insuperable difficulties in the way of a satisfactory classification. The case in our opinion must be simply considered as one of myelosarcomatosis, since the tumor is distinctly myeloid in type. It will be remembered that no characteristic blood picture was presented during life. In certain places the sections, especially of the splenic vein, show large clusters of these tumor cells, but evidently these cells, at least as judged through two examinations of the blood, were not regularly circulating in the blood. According to Borst's classification, at least for the present, the diagnosis of myelosarcomatosis must be made. In view of this it may be wise to review briefly Borst's recent article upon the classification of the sarcomas.

According to Borst, the sarcomas arising from the

lymphoid and myeloid tissues of the hemapoietic system, the so-called hematoblastic sarcomas, are of great interest, since they approach in type many diseases whose classification, in the present state of our knowledge, presents great obstacles. Recently he has emphasized the difficulties which exist in distinguishing the inflammatory growths from real tumor processes, and drawn attention to the existing tendency to classify the disease processes which anatomically resemble new growths with the infectious granulomas. According to Borst, any classification of these tumor processes must be considered a temporary makeshift. He divides the hematoblastic sarcomas into two broad groups.

In the first group belong the primary solitary tumors which are malignant. A variety of names has been given to such tumors: Lymphoma sarcomatosum; Lymphocyto-blastosarcoma, or Sarcoma lymphaticum, lymphadenoides or lymphomatosum, or simply Lymphosarcoma, and, by Ribbert, Lymphocytoma. These tumors in their structure resemble lymphatic tissue in a more or less complete manner as to reticulum, and as to the lymphocytic character of the tumor cells.

The tumors vary among themselves as to the predominant character of the cells, in some cases the cells resembling the large cells found in the germinating centers of the lymph nodes, rather than the small lymphocytes. These tumors spread, as do the typical sarcomas, by means of the lymph or blood stream. Such sarcomas arise from various places and organs, especially the lymph nodes, spleen and marrow. Another tumor with the same characters in regard to its origin, growth, and manner of spreading, resembles in its structure myeloid tissue. These tumors arise from the marrow and possibly, according to Borst, from the periosteum, as primary soli-

tary tumors, the so-called myelocyto-blasto-sarcoma, or, briefly, myelosarcoma or myelocytoma.

In rare cases these tumors have even a closer resemblance to the parent tissue, by the formation of rudimentary blood-forming islets; that is, by the presence of hematoblastic cells, these tumors representing the so-called hematoblastic sarcomas of Hanseemann, Albrecht, and Borst.

The second group of tumors, which stand in marked contrast to the tumors of the first group, is called by Borst primary multiple systemic sarcoma, or sarcoma-like new growths, which Sternberg has lately reviewed. In this large group the tumor process is confined to one portion, or to the whole, of the blood-forming system; that is, the myeloid or lymphatic system, the process appearing simultaneously in many widely separated places, or beginning in one place and then rapidly spreading to other places in the same kind of tissue, or in other tissues which are functionally similar. In this way a true metastatic process may be simulated. The difficulty in eliminating this factor is increased because of the presence in many organs of small microscopic lymphoid nodules which do not in the strict sense belong to the blood-forming system; namely, the lymphatic apparatus of the mucous membranes, liver, kidney and lung.

Sternberg and others have recently called attention to the normal occurrence of myelocytes in the spleen and lymph nodes. Furthermore, certain organs, especially the liver, spleen and kidneys, in their fetal life have blood-forming functions, red and white blood cells being manufactured in these situations, and under certain circumstances this may occur in later extrauterine life. It is therefore not surprising that these organs, the liver, spleen and kidney, are affected in such systemic diseases.

In other words, the lymphocytes, myelocytes and erythroblasts occurring in tumors may develop *in situ*, instead of being carried from a distant focus.

Sternberg and Borst are of the opinion that the true sarcomas should be separated from the leukemias and pseudoleukemias and the multiple myelomas. The myelomas show in their macroscopic appearance a striking similarity to the cells of the bone marrow from which they have been developed. In these affections there is thus missing the aberrancy from the normal type shown by the cells of the real sarcomas, a diagnostic feature which has been so much emphasized. The process is an example of a systemic tumor-like hyperplasia, unassociated with malignancy, local destruction and replacement of old tissue by new tissue, or with metastases. These tumor-like processes are made up either of myeloid tissue, in other words, a myelogenous leukemia, or of lymphatic tissue. The close relationship between the leukemias and the pseudoleukemias is at the present time recognized, as the latter can turn into the former, the difference being purely quantitative in respect to the changes in the blood picture presented in either disease. Thus, when the white blood cells formed in the marrow enter the blood system the disease is leukemia; when they do not it is pseudoleukemia.

The general pathological status of these so-called systemic diseases has not been positively determined. It is possible, according to Borst, that some may later be grouped with the infectious granulomas, in the same way that we now recognize the false pseudoleukemia; in other words, the diffuse lymph node tuberculosis. The other systemic diseases of this class which have not an infectious basis should be, according to Borst, classified as homotypic true blastomas, making them analogous to

the benign connective tissue new growths, as an example, the so-called multiple fibromatosis of the nerves.

Opposed to these homotypic systemic tumor-like processes are the heterotypic malignant and infiltrating tumors which form metastases. These multiple primary systemic malignant tumors have been classified under the name of sarcomatosis. They have been separated into two groups, the myelo- or lympho-sarcomatoses, according to Sternberg, on the basis of the tissue from which they have originally sprung or which they resemble. In some of these tumors the atypical cells have entered the blood current. Such cases are referred to then as leuko- or chloro-leuko-sarcomatoses, or, better, as lympho- or chloro-sarcomatoses with a leukemic blood picture. When the cells possess granules, one speaks of a myelosarcomatosis. When the cells do not enter the blood current, one speaks simply of lymphosarcomatosis or of myelosarcomatosis. According to Borst, a tumor of the latter class has not yet been recognized, but it seems probable that it will be found.

Our case does not correspond to this type of Borst, inasmuch as the cells have no granules. Nevertheless, we feel justified in placing the case in this group of myelosarcomatosis, on account of the myelogenous character of the tumor cells. It is best not to call it a myeloma, since this name has been applied only to processes involving the bone marrow alone. Nevertheless, our case resembles in a great many respects a malignant myeloma, in other words, a myeloma which has formed metastases.

BORST. *Beiträge z. path. Anat. u. allg. Path.*, Bd. XXXIX, 1906.

STERNBERG. *Ergebnisse d. allg. Path.*, Lubarsch u. Ostertag. Neunter Jahrgang, II Abt., 1903.

Discussion.

Dr. E. LIBMAN thought that this case reported by Dr. Norris was remarkably interesting. If more cases which are at present grouped as lymphosarcoma were studied with care it would be possible to arrive at a better classification. The cells which Dr. Norris had described probably corresponded to the myeloblasts. Since the cells in Dr. Norris's case possessed no granules, Dr. Libman suggested that the case might be called a myeloblastoma. It was interesting to note that while the tendency had been to group separately cases of leukemia having small lymphocytes and those having the large cells (corresponding to the myeloblasts), and Sternberg had claimed that the leukemias with small lymphocytes should be classed as leukemias and those with large cells as sarcomata, yet recently a case of leukemia had been described by Luksch in which both types of cells were present. This would involve still further classification.

Dr. JAMES EWING said that he had had the opportunity to study the cells in this case in some detail and thought that the attempt to classify this tumor by a minute study of the cells would be unsuccessful. These cells were of very large dimensions and were not like any cells in the normal human body. Any attempt to trace the origin of the cells by their morphology was hopeless. If any satisfactory classification of this group of tumors was ever to be reached it must be based upon the general biological features and not so much on the minute characters of the cells.

A CASE OF PRIMARY CARCINOMA OF THE
BILE DUCTS.

A. M. PAPPENHEIMER, M.D.

Dr. A. M. Pappenheimer presented briefly a case of primary carcinoma of the common bile duct, which showed some rather interesting features. He was indebted to Dr. Nammack for permission to use the clinical records.

The patient was a butcher, fifty-three years of age, who was admitted to the Fourth Medical Division at Bellevue Hospital, on October 20, 1906. He was said to have been an excessive drinker of beer and whiskey. The symptoms for which he was admitted dated back three months, when he first noticed that he had become jaundiced; shortly afterward, his abdomen began to swell. The icterus deepened gradually in intensity, and his abdominal distention became more marked. At the same time his appetite failed, and he began to lose weight and strength. He had no severe abdominal pain at any time and suffered only from a sensation of heaviness and distention in his abdomen. His bowels were constipated until within three days of admission, when he had a sharp attack of diarrhea. Following this there was complete obstipation, unrelieved after his entrance into the hospital by cathartics or enemata. There had been no vomiting or bloody stools.

Upon admission the patient was very weak, prostrated, somewhat emaciated, and slightly delirious. There was marked icterus of the skin, scleræ and mucous membranes. The tongue was dirty and heavily furred; the breath foul. The heart was displaced upward; and the sounds were feeble and irregular. The pulse was small, weak and arrhythmic. The lungs showed general

sibilant and moist rales, with dulness and diminished respiratory murmur at both bases. The abdomen was much enlarged and distended. There was a diffuse fulness in the epigastric region, a shallow depression across the umbilicus, and, again, a diffuse prominence in the lower portion of the abdomen. Percussion showed general tympany. There was rather marked general tenderness on palpation. The abdominal wall was tense, but there was no muscular spasm. None of the viscera were palpable, and no tumor masses could be distinguished. Liver dulness began at the 4th rib in the right mammary line, and extended not quite to the free border. The spleen did not appear to be large on percussion, and could not be felt.

The urine showed a trace of albumin, occasional hyalin and granular casts, and bile in large amount. The blood showed a leucocytosis of 28,000, and a slight secondary anemia.

The patient lived three days after admission, dying with symptoms of cholemia. He became, first, very delirious, then lethargic and comatose. The abdominal distention increased rapidly, and as his bowels remained obstinately constipated, a suspicion of intestinal obstruction was entertained. His condition, however, did not justify an exploratory operation.

At the necropsy, performed six hours after death, there was found intense light yellow icterus of the skin and conjunctivæ. All the body tissues and fluids were bile stained. The abdomen was prominent and tense; the panniculus scant. The peritoneal cavity contained several liters of turbid, dark yellow or brownish fluid, in which floated large yellow fibrin flocculi. The omentum was rolled up over the surface of the liver, and was adherent between the anterior surface and the diaphragm.

The intestines were much distended with gas, displacing the diaphragm upwards. The peritoneum in a few places showed slight recent fibrinous deposits. The liver extended not quite to the costal margin. The heart and lungs presented no noteworthy lesions. The liver was slightly reduced in size, and greenish in color; and the surface was finely granular. The organ was very firm, and on section showed a fine, irregular cirrhosis. The large intrahepatic bile ducts appeared to be dilated, and were filled with dark green bile under considerable pressure. The gall bladder was much distended, projecting about three fingers' breadth below the liver, and lying with its long axis almost parallel to the lower border. The wall of the gall bladder appeared slightly thickened; but there were no adhesions. Upon opening the duodenum, thick, greenish bile escaped from the papilla, without pressure upon the bladder. Beneath the mucous membrane, the transduodenal portion of the common duct could be seen and felt as a rigid, thick-walled cylinder.

After hardening, a series of transverse sections was made through this portion of the duct, including the overlying duodenal wall and the adjacent pancreatic tissue. It was then found that this portion of the common duct for a distance of several centimeters proximal to the ampulla showed a diffuse and uniform thickening of the wall. The tissue of the duct was grayish white and very firm. There was no infiltration of the duodenal wall, and only in one section did the new tissues appear to encroach slightly upon the head of the pancreas. The wall of the duct measured about 5 to 7 mm. in thickness. The lumen was slightly narrowed, but was nowhere completely stenotic. A small probe could be readily passed up through the papilla. The ampulla itself

appeared somewhat rigid and thickened, the mucous membrane normal. Wirsung's duct was found to open into the ampulla and was patent.

The common duct proximal to the thickened portion, as well as the cystic and hepatic ducts, was dilated to the size of one's thumb. At one point, about 2 cm. below the junction of the cystic and hepatic ducts, the common duct showed slight thickening of the wall. The overlying mucosa was normal. The periportal and peripancreatic lymph glands were moderately enlarged, but on section showed no evidence of malignant involvement.

The remainder of the organs showed no features of special interest. No secondary malignant deposits were found in any of the viscera. The small intestine contained colorless, rather greasy, fecal matter; but in the large intestine the stools were bile stained, showing that complete biliary obstruction had not occurred until shortly before death. To explain the acholic feces in the small intestine, in view of the fact that the duct at autopsy was patent throughout we may assume a muscular spasm in the infiltrated portion, as has been suggested by Rolleston, or possibly an interference with the normal peristalsis along the ducts, or a transient plugging of the orifice of the ampulla with mucus or inspissated bile. It is very likely that atony of the gall bladder from over distention may also have been a factor.

Cultures made from the gall bladder on ascitic agar proved sterile. On opening the bladder the mucous membrane was found to be normal; there were no calculi.

Histologically, the thickening of the duct proved to be due to an infiltrating scirrhous carcinoma of the columnar celled type, undoubtedly taking its origin from the mucous membrane of the duct. The acinal structure

was fairly well retained, even to a considerable depth in the wall; but lying in the lymph spaces of the stroma were solid nests or islands of closely packed cells, in which the columnar form was no longer discernible. The cells which composed these islands showed some very remarkable features. Many of them were exceedingly large. Frequently the cells, crowded together, had lost their individual outlines, and formed large syncytial protoplasmic masses containing a number of swollen vesicular nuclei. There were also some curious structures within these cell nests. In the midst of a group of cells there was frequently to be found a sharply outlined circular or spherical space, crowding the adjoining epithelial cells with their contained nuclei into crescentic shape. Within this circle lay a single epithelial cell, showing always more or less degenerative change. At a later stage of the same process there was a very large but clearly circumscribed vacuole in which could usually be found the degenerated but structureless remains of an epithelial cell.

The tumor was found, in sections from one block, to infiltrate the pancreas for a short distance, penetrating the lobules as well as growing into the interlobular connective tissue. The pancreatic ducts were not dilated, and were quite normal in appearance, proving that Wirsung's duct was not obstructed by the growth. In confirmation of this there was found in a section through the ampulla itself only an adenomatous hyperplasia and no carcinomatous change.

The liver showed an advanced cirrhosis of irregular type, with a rather cellular connective tissue. There was considerable stasis of bile in the bile capillaries, and in places, bile pigment within the liver cells. On the other hand, the bile ducts in the portal spaces did not

appear in the sections to be greatly dilated. A few small areas of necrosis were found, in what portion of the lobule was not clear. There was some evidence of acute inflammatory change, as polynuclear leucocytes were found throughout the section between the liver cells and in the periportal spaces.

Discussion.

Dr. EDWIN BEER asked Dr. Pappenheimer whether these peculiar cells which he had described resembled the "epidermoid" changes occasionally seen in the bladder.

Dr. PAPPENHEIMER said that he had seen no illustrations of this condition though he had seen it described. One author called it a metaplasia of the cells with the formation of prickle cells in the gall-bladder. He did not think that this case showed anything of this sort.

Dr. F. S. MANDLEBAUM said, in regard to the type of cells which Dr. Pappenheimer had mentioned, the crescentic cells, that on two or three occasions he had met with cells of similar type. One case which he remembered distinctly was a primary carcinoma of the rectum where nearly all the cells were of this type. He had for a long time been puzzled as to the significance of this find, and thought it was due to a dropsical condition of the cell and mechanical pressure on the nucleus. In the past few months he had met with two other cases, both in the stomach, presenting this same type. One occasionally sees it in colloid tumors. He did not mean that this was such a case, but cells of this type were not uncommon.

TWO CASES OF FATAL HEMORRHAGE FROM LACERATION OF THE MUCOSA OF THE OESOPHAGUS BY VOMITING.

OTTO H. SCHULTZE, M.D.

Dr. Otto H. Schultze presented two specimens from cases which were quite similar, showing a very rare lesion; at least they were the only cases of the kind which he had seen. The specimens were obtained from male alcoholics; in both the cause of death was hemorrhage. In each cadaver the stomach and small intestine were found filled with blood. The only discoverable source of the hemorrhage was, in the first case, two longitudinal lacerations of the mucosa of the oesophagus at the cardiac orifice; and, in the second case, two similar lacerations at about the level of the cricoid cartilage. The lacerations were quite fresh, between two and three cm. in length, about five mm. in width at the middle and tapering to an acute angle at each end. The microscopical slide from the first case showed a laceration of the mucosa with no pathological process to account for it. The submucosa at and on each side of the laceration was infiltrated with blood. There was a beginning reaction in infiltration of leucocytes.

The first case, an adult male, was admitted to the House of Relief, June 14, 1904, and died the following day. He had been on a prolonged spree and had come to New York on a coastwise steamer. He had been seasick on the voyage and continued vomiting. While under observation he vomited blood.

The second case, an adult male, was admitted to Bellevue Hospital, August 24, 1905, and died within twenty-four hours. Very little history was obtainable except that of continued vomiting.

There were no varicose veins in these cases, no lodgement of foreign bodies, nor passage of any instrument. The only etiological factor at hand in both cases was the vomiting which in turn was most probably due to alcoholism.

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DR. F. S. MANDLEBAUM, *President*.

GANGOSA. AN UNUSUAL FORM OF TROPICAL ULCERATION INVOLVING THE NASO-PHARYNX.

JOHN A. FORDYCE, M.D.

My attention was first called to an unusual form of ulceration in a native of Panama involving the nares, pharynx and larynx, and implicating by extension the upper lip and nasal duct. The history of that patient is briefly as follows:

He was a negro, aged forty, and was admitted to the City Hospital in 1904. His history was negative until six years previously when his trouble began with an

annoying and offensive muco-purulent discharge from his nose and a gradually increasing difficulty in breathing. A year later small ulcers appeared about the nasal orifices and the disease extended until it involved the upper lip and destroyed the septum, the anterior nares and the uvula. The soft palate presented a worm-eaten appearance and his larynx and pharynx showed old cicatricial contractures with here and there ulcerating areas. Just below the inner canthus of the right eye there was also a small ulcerated area resulting from an extension of the infection through the nasal duct. A diagnosis of syphilis was made and mercury was given internally, by inunctions, and hypodermatically, and potassium iodide in increasing doses until the limit of tolerance in more than 300 grains daily was reached. The failure to respond to treatment suggested a possible tuberculous disease and the patient received two injections of tuberculin, neither of which produced any reaction. Smears and tissue were examined for tubercle bacilli and guinea pigs were inoculated, but without result. Histologically, the picture was a granuloma of unknown nature. Bacteriological examination produced only Gram positive cocci.

I then thought the process might be a form of tropical ulceration which was contracted while the patient resided in Panama, and my view was strengthened by reading the report of Breda of Padua, Italy,¹ on nasal ulcerations in Italian emigrants returning from Brazil, to which he gave the name *Frambæsia brasiliiana* or *boubas*. The affection was described as distinct from syphilis and yaws, beginning as a bulla or pustule which gave rise to remarkably indolent ulceration with sharply defined infiltrated margins and a gray nodular base. It involved

(1) *Gior. Ital. del Mal. Ven. e della Pelle*, XXXV, 1900, p. 489 and *Arch. f. Derm. u. Syph.*, XXXIII, 1905, p. 3.

not only the skin but the mucous surfaces, especially the palate, throat, larynx and trachea. The voice was profoundly modified early in the affection. Anti-syphilitic medication and the tuberculin test were negative. In some of its essential features the malady described by Breda corresponded to this case and forcibly suggested a tropical ulceration of unknown nature. Shortly after, U. S. Naval Surgeon W. F. Arnold saw the photographs of the patient in question and recalled similar cases he had seen in the Island of Guam. The narrative of his experience there still further strengthened my reasons for regarding the disease as a distinct entity and jointly we published the case as "An Undetermined Form of Tropical Ulceration Involving the Nose, Pharynx and Larynx."²

In February, 1906, Dr. Leys (Surgeon U. S. N.) reported, in the *Journal of Tropical Medicine*, a similar condition which he saw in the Island of Guam, as Rhinopharyngitis mutilans. He said it existed throughout the Ladrone and Caroline Islands and had been reported in Fiji, British Guiana, Jamaica, Dominica, Italy and Hawaii. The natives connected its etiology with rotten sun-dried fish. Medical new-comers and casuals have looked upon it as a form of (1) leprosy, (2) hereditary syphilis, (3) tertiary syphilis, (4) tuberculosis and (5) a sequel of yaws. In his reasons for believing it to be an independent affection he argued that lepers are not known to suffer from this peculiar form of ulceration and that the gangosa cases show no sign or symptom of leprosy. As against hereditary syphilis, it appears in healthy well-developed persons of all ages with no signs of syphilis on their own persons or in other members of the family. Acquired syphilis is extremely rare on the island and the appearance

(2) *Jour. of Cutaneous Dis*, XXIV, 1906, p. 1.

of the primary lesion of rhinopharyngitis in otherwise healthy children of healthy parents at three, four and nine years of age also excluded tertiary syphilis. As to a tuberculous origin, the victims have no signs of tuberculosis elsewhere. Instances have been observed of several members of the same family all afflicted with only the peculiar lesions of this disease. As an argument against its being a sequel of yaws, the latter is very common in the tropical world, while rhinopharyngitis is not and is never met with in some of the localities where yaws is especially prevalent. A few of the cases give a history of yaws, but the majority do not.

Dr. Mink and Dr. McLean³ (Surgeons U. S. N. Station, Guam) reported the disease as Gangosa (Spanish for muffled voice) and gave a number of illustrations showing the mutilations produced by it. They say it has existed in Guam for at least one hundred and fifty years and probably much longer. During the past year one hundred and twenty-five cases have been under examination, many under compulsion, the total number in the island being estimated between two hundred and two hundred and fifty. The majority of cases begin during the second and third decades, with a preponderance among women. Pure blood natives are usually attacked, which very likely is explicable on hygienic and dietetic grounds. Heredity is not a factor in its transmission and Mink and McLean consider the native food theory improbable. Regarding a relationship between syphilis and yaws, their observations agree with Leys's. They believe that there is a specific infecting agent and that flies are an important factor in its transference. But few cases have come to notice in the early stages of the disease, and in these there appeared to be a mild tonsillitis,

(3) *Jour. Amer. Med. Assn.*, XLVII, 1906, p. 1166.

pharyngitis and laryngitis, a slight rise of temperature and soreness in the posterior nares and pharynx with stiffness of the muscles of deglutition. On the third day a patch of yellowish gray membrane, elevated, thick and extremely tenacious was observed and within twenty-four hours the typical ulceration was established. The ulcer had a punched-out appearance with undermined edges and rapidly increased until the uvula and soft palate were perforated by the seventh day. After the first week the disease progressed steadily, the bony and soft parts being destroyed with equal ease. The active stage may vary from one to seven years; in a few cases which have never been quiescent the shortest has continued for ten and the longest for thirty-five years. Periods of activity and quiescence may alternate; and when inactive, cicatricial tissue replaces the inflammatory zone, from which there is an abundant and offensive discharge. At no time is the general health materially affected. It is never fatal in adults and death usually takes place from some intercurrent disease. A fulminating type occurs in children under five years in gangotic families, in which the picture closely resembles diphtheria and death usually supervenes within forty-eight hours. The deformity resulting from this disease is very marked, all the tissues attacked being entirely or partly destroyed. The destruction of the affected area by local treatment in the beginning of the affection limits its progress, but after it has advanced nothing effectually influences it.

The disease is attracting a good deal of attention just now and is having serious consideration by the officials of the army and navy departments. During the eight years of American occupation the patients were not segregated, as formerly by the Spaniards, and the disease spread alarmingly. Now a colony has been established at

Ypao; but in a recent letter to the department, the Governor of Guam stated that he would be forced to release the gangosa as well as the leper patients unless he was allowed \$9000 a year for the maintenance of the colonies.

The tissue presented was sent to me by Dr. Mink and Dr. McLean. It is the only case that they have had for autopsy, a boy of eighteen in whom death resulted from native epidemic asthma.

The left half of the nose and part of the upper lip were destroyed and were replaced by a triangular opening leading to the pharynx. There was a perforation of the soft palate and the tonsils and faucial pillars were replaced by scar tissue. The nasal cavity was the seat of an extensive destructive ulceration, the septum and turbinated bones having entirely disappeared.

A small piece of tissue removed from the edge of the naso-labial ulceration of this specimen showed the lesion to be identical with that of the case from Panama. It was situated in the derma and hypoderm and consisted of a delicate reticulum with an infiltration composed largely of lymphocytes, plasma, mast and giant cells. The vessels were the seat of an endarteritis, some of them being entirely occluded. In the deepest layers of the derma independent foci of the above mentioned cells were seen. An examination for organisms has so far revealed only numerous Gram positive cocci and bacilli in the superficial layers of the skin.

Summary: Although the histological picture strongly suggests a local form of tuberculosis, we can, it seems, exclude that disease by the manner of its onset, its well-defined clinical course and the total absence of constitutional manifestations. It would not be possible to assume that a local form of tuberculosis would preserve the distinct type which is here presented, the clinical appearance

in various members of a family or in subsequent generations always being identical. In Breda's cases, which resembled the one in question as well as my own, the tuberculin test was negative, and although these tests may not have been conclusive, they add somewhat to the value of the negative evidence. Then too, the fulminating type which is met with in children and results fatally in so short a time could scarcely be looked upon as tuberculosis. In the light of the work which has been done, it is fair to claim that we have a type of disease distinct from tuberculosis, leprosy and syphilis, the nature of which is yet to be revealed by bacteriological and experimental investigations.

Discussion.

DR. JAMES EWING asked whether any attempt had been made to transfer this disease to lower animals. The study of such an interesting and obscure complaint, which afforded but little opportunity for experimental study, might find its first real step of progress in the experimental production of the disease in animals.

DR. F. S. MANDLEBAUM asked whether the sections resembled in any way those of rhinoscleroma. Not that the case clinically had any resemblance to this condition, but it was known that these cases might involve the pharynx and the deeper parts without affecting the nose proper, causing a rather marked ulceration. The description given of the histological findings in gangosa, though not resembling entirely those of rhinoscleroma, might lead one to think that a condition of that kind might be at hand.

DR. FORDYCE said in regard to animal inoculations that so far only one case (Panama) had come under observation in this country, material from which had

been inoculated into two guinea-pigs. The one inoculated under the skin developed a slowly spreading ulceration which did not have the histological structure of the original lesion. In regard to the resemblance of the case to rhinoscleroma, Dr. Fordyce said that clinically there was none, neither was there any similarity histologically, nor was the organism found in rhinoscleroma present in his cases. The infiltration was more like that of tuberculosis or syphilis.

A CASE OF HEPATIC ADENOMA ORIGINATING FROM AND SIMULATING LIVER PARENCHYMA.

HARLOW BROOKS, M.D.

Dr. Harlow Brooks presented a case of hepatic adenoma, the history of which was briefly summarized. The patient was a boy of fourteen years who gave a history of four years standing of progressive anemia associated with increasing jaundice which did not yield to treatment. After four years without treatment, except such as he got in a charity school in which he was placed, he entered St. Vincent's Hospital. At the time of admission he was very much emaciated and there was a marked jaundice and a profound cachetic condition. In the hepatic region it was easy to palpate a cystic mass about the size of a man's fist. The child had evidently not developed either physically or mentally for the last four years. The tumor was supposed to be a gumma and the child was put on antisyphilitic treatment without result. The anemia progressed and as the outcome seemed certain death, the surgeons consented

to make an exploratory laparotomy. The tumor exuded a small quantity of material, whitish pink in color, which on microscopic examination showed what was taken to be necrotic liver cells. This child died two weeks after the operation.

At autopsy nothing of interest was found outside of the liver.

The liver presented a tumor mass about the size of a man's fist on the upper surface. A firm whitish material formed the substance of the tumor and there was no cyst. The portal vein was completely occluded by solid white and pinkish tissue. All through the substance of the liver there were solid pearl white growths, strictly confined to the ramifications of the portal veins. In a few places these thrombosed branches showed evidences of canalization and a small amount of circulation had been established through the new formed vessels. The microscopical examination showed the whitish tumor material which filled the portal vein to be so much like liver tissue that it was impossible to tell whether one was examining tumor tissue or liver tissue. As the structure was so like normal liver tissue the tumor had been called an adenoma. The tumor cells presented marked fatty degeneration and glycogenic infiltration was demonstrated. In some places there was a distinct lobular arrangement. Large, wide open cavities were situated between the liver cells. Dr. Brooks thought the members would agree with him that this was a case of adenoma springing from the parenchymatous tissue of the liver; the tumor simulated liver tissue but was not malignant and set up no metastases and did not destroy the liver tissue. It was restricted to the portal vein. So far as the literature had been looked over no similar case had been found. Most liver adenomata originate in the bile

ducts. There was no reproduction of bile ducts in this tumor so far as could be found. The gross anatomical diagnosis was hepatic hypernephroma; but the typical structure completely excluded that growth.

Discussion.

DR. F. C. WOOD said that he had in his collection a specimen of adenoma of the liver resembling in some details the specimens shown by Dr. Brooks. He never felt sure when examining a section which portion was adenoma and which normal liver tissue. On gross section one could see a distinct capsule to the adenomatous mass; which was also whiter and somewhat more dense. Microscopically it was difficult to tell the difference. The cells in the adenoma were a little larger and more irregular than the normal.

DR. F. S. MANDELBAUM said that he had thought Dr. Brooks' case might resemble a case which he had had the good fortune to examine recently, and he had brought some photographs of his case with him. Although Dr. Brooks' case had proved to be quite different, and Dr. Mandelbaum intended to present his in detail at some later time, he still thought it would be worth while to say a few words about it. This case of adenoma of the liver was in a man of sixty-two, who was treated for some supposed malignant neoplasm of the abdomen. He never was operated upon. At autopsy the liver was found to weigh 14.5 pounds. The entire organ was made up of nodules varying in size from two to twenty millimeters; and while a few of the nodules seemed to present normal liver substance, the great majority were adenomatous in structure. Some of them showed beginning carcinomatous proliferation. It was almost impossible to tell from the gross appearance what nodules were adenoma

and what showed beginning carcinomatous changes. Dr. Mandlebaum also had a slide which showed very plainly the peculiar type of the growth. One of the photographs, low power, magnification 9 times, showed that the liver substance was entirely made up of nodules of various sizes. Other photographs showed the typical adenomatous arrangement, one showing the ordinary type, others showing dilated acini containing retained bile. Another photograph showed the change into carcinoma and still another showed carcinoma of liver tissue. In this case the adenoma beyond any doubt arose from the liver cells. This fact is well known, though former writers supposed that it nearly always arose from the bile ducts. At the present time it has been proven without doubt that adenoma of the liver may arise from liver cells.

DR. HORST OERTEL asked Dr. Brooks whether the rest of the liver substance was histologically normal.

DR. BROOKS said that the rest of the liver substance showed the changes of a profound passive congestion, as would be expected from thrombosis of the portal vein. Otherwise the liver tissue was normal; that is, it showed no deviations from the normal structure. The boy presented no congenital malformations in any way. Dr. Brooks had been interested in hearing of Dr. Mandlebaum's case and was encouraged to know that it was believed that tumors might spring from the parenchyma of the liver tissue, and might simulate liver tissue so completely.

BLOOD COAGULATION.

G. W. ROSS, M.D.

Dr. G. W. Ross, of Toronto, Canada, described, by invitation, the method devised by Professor Wright for estimating the coagulation time of the blood.

EXPERIMENTAL CEREBROSPINAL MENINGITIS IN MONKEYS.

SIMON FLENNER, M.D.

I wish to show a series of microscopic slides prepared from the brain and spinal cord of monkeys inoculated with *Diplococcus intracellularis*. They bear, I think, a close resemblance to similar preparations made from the nervous system of certain acute cases of epidemic meningitis in man. The experimental disease is produced by inoculating monkeys into the spinal canal, with cultures of the diplococcus. The first symptoms appear in a few hours, and they progress until death, which occurs as soon as twelve hours or as late as fifty hours after inoculation. The lesions vary in degree according to the length of survival and of other causes. The period of survival depends partly upon the dose of the culture and partly upon the resistance displayed by the animal. A certain number of the monkeys recover from the effects of the inoculation. By re-injecting, at intervals, some of the monkeys with carefully graduated doses of the culture, a more prolonged form of infection is produced, to which they eventually succumb. These animals show subacute inflammation of the meninges, heavy exudates, and in some instances, widely dilated cerebral ventricles.

The histological appearances are chiefly those of acute fibrinopurulent meningitis and acute encephalitis. The inflammatory exudate is abundant over the lower part of the spinal cord, the medulla and other basal cerebral parts, and in the sulci between the convolutions. Small hemorrhages are not uncommonly present in the membranes and brain. The encephalitis arises (*a*) by direct invasion of the cortex from the inflamed pia-arachnoid, and (*b*) by extension from the inflamed intracortical blood vessels. Thrombi of leucocytes and fibrin, or of agglutinated red blood corpuscles are seen occasionally in these vessels. In the examples of subacute inflammation the large cells of the connective tissue spaces of the arachnoid, etc., multiply freely. Among the special lesions are, acute endarteritis, leucocytic invasion of the dura of the spinal cord at the point of inoculation, and beyond the olfactory lobes as far as the ethmoid bone, inflammation of the intervertebral ganglia, optic nerves, etc.

Diplococci are abundant in all the exudates except where death resulting from a single inoculation is greatly delayed. The diplococci are largely taken up by leucocytes, and the cells and included diplococci resemble in all respects the diplococci-containing phagocytes found in the exudate in the human disease. Cultures are usually successful, but they may fail in the case of those animals which survive long periods or which are kept in the refrigerator for many hours after death.

Discussion.

DR. F. S. MANDLEBAUM asked Dr. Flexner whether any embedding agents had been used in those cases in which he had had difficulty in finding the organisms.

DR. FLENNER said that the general procedure had been to put bits of tissue into Zenker's fluid and embed them in celloidin and paraffin. His best results had been with the paraffin sections.

DR. MANDLEBAUM said that he had himself found difficulty in staining organisms in tissue which had been embedded in celloidin. When the celloidin was first removed from the tissue by oil of cloves, the organisms subsequently could be stained; while in other material where the celloidin had been allowed to remain in the sections the organisms were not demonstrable.

THE THERMOSTABLE ANTICOMPLEMENTARY CONSTITUENTS OF THE BLOOD.

HIDEYO NOGUCHI, M.D.

Blood serum contains normally certain principles which inhibit serum hemolysis by interfering with the action of complement. In the case of most sera, the anticomplementary action appears only after heating to 56° C. or higher.

The inhibiting action of this principle is directed against alien as well as native complements, and is non-specific in character.

It would appear as if the inactivation of serum at 50° C. or thereabouts were due to a partial liberation of the antilytic principle which just about suffices to neutralize the action of the native complement. As the temperature of the serum is raised, up to a certain point, more and more of the antilysin is set free, until the serum comes to contain an overplus, in excess of the quantity neutralizing its

own complement, which is capable of interfering with the action of additional native or alien complements.

Serum heated to 90° C. is less antilytic than serum heated to 70° C., either because the antilysin has entered into new, more stable compounds which prevent its action, or, as is more probable, because of the liberation from the serum of a second group of principles in themselves hemolytic directly, or indirectly by increasing the power of serum hemolysins (auxilysins). This latter action tends to mask and to suppress the inhibitory influences of the antilysin.

The antilysin is removed from serum by digestion with many kinds of blood corpuscles which, apparently, absorb the principle. While, by reason of this treatment, the serum is deprived of its inhibitory power, the corpuscles have acquired greater resistance to serum hemolysins.

By treating blood serum and corpuscles with ether, the antilysin can be extracted. The ethereal extract, freed from lecithin and certain related bodies, contains the antilysin in a concentrated but not in a pure form, which can now be taken up in saline solution in which it dissolves.

The saline solution of the antilysin, which for convenience has been demonstrated "protectin," behaves in all respects like the native antilytic sera, except that it is uninfluenced by temperatures of 90° C. or even higher temperatures. Protectin inhibits serum hemolysis directly by neutralizing complement and indirectly after absorption by corpuscles by increasing their resistance. Hence, it is highly probable that the antilytic principle of heated serum and protectin extracted from serum and corpuscles are the same substance.

Thermostability is one of the characteristic properties of protectin. Serum and corpuscles, first dried, may be heated to 150° C. without losing the protecting principle, and the principle persists in such heated products for at least two years. Protectin in solution is unaffected by a temperature of 100° C. maintained for one hour, and suffers only a slight reduction in activity at the expiration of two hours; while a temperature ranging from 135° to 150° C. brings about marked reduction in activity in protective power. As these alterations are produced by high temperatures the reaction of the solution changes from acid, through neutral, to alkaline.

Discussion.

DR. R. WEIL thought that it would be well to draw attention to the fact that Dr. Noguchi's conclusions did not hold universally. He had done work on the hemolytic action of extracts of organs and had found it possible by dissolving the red corpuscles in water to extract a complementary substance which acted very powerfully. So that it was not fair to look upon the red cells as containing only anticomplementary substances, for they contain very powerful complementary substances also. Heating the red corpuscles changed their action very markedly. At 56° the action was not affected, at 80° it disappeared, at 100° it became antihemolytic. In what way it was antihemolytic it was impossible to say at present. As regarded heating the serum, Manwaring had shown that the effect of heating serum was in some way to produce a body which increased the hemolytic action of the amboceptor group; in other cases it was anticomplementary. In the organ extract work it has been found that serum is always antihemolytic. The same thing has been found by other workers who have tested Manwaring's

results, but who have gone further by testing the effect of heat. They found uniformly that serum did not lose its power.

Dr. SIMON FLEXNER said that he did not think there was anything seriously contradictory in these experiments. As regarded Dr. Noguchi's report, the particular point was that one could extract from serum, from corpuscles, and from organs, anticomplementary substances that had a very powerful anticomplementary action. They were of chemical nature and were very stabile substances. Thus far they had appeared in very small amounts, though in quantities large enough to work with and to determine that they were anticomplementary substances. They could be taken up by the corpuscles and the resistance of the corpuscles increased.

DEMONSTRATION OF SPECIMEN OF FILARIA SANGUINIS HOMINIS: A REACTION FOR CODEINE IN THE URINE.

F. C. WOOD, M.D.

Dr. F. C. Wood demonstrated a specimen of *Filaria sanguinis hominis* in the blood of a patient from Barbadoes.

Dr. Wood also called attention to the fact that he had observed in the urine of two patients a red coloration with chloroform while doing Obermeyer's test for indoxyl. This color he had never seen except in persons taking large quantities of codeine. Control of the test had shown that it was not indigo red, not iodine, and not skatol nor urobilin. The color could not be produced in dogs' urine

by large single doses of codeine, nor was it present in the urine of a diabetic patient who was taking one grain of codeine in twenty-hours. Dr. Wood was not willing to state that the color was necessarily due to codeine, but he thought that possibly by calling attention to the matter it might develop that others had had the same experience. An attempt had been made to isolate the alkaloid from the colored chloroform extract, but up to the present such tests had not been positive.

A CASE OF PRIMARY CARCINOMA OF THE LIVER.

JAMES EWING, M.D.

Dr. James Ewing presented a case of primary carcinoma of the liver, exhibiting photographs and sections, and saying that as several tumors of the liver had recently been presented before the Society, and as this case showed some special points of interest, he had thought it worthy of presentation. The clinical history of these cases was apparently rather characteristic in the fact that very few showed any symptoms, and this particular case was no exception. The patient was an old man of sixty-five, who had had no symptoms of note until the day of his death, which occurred suddenly, apparently from abdominal hemorrhage. At autopsy the seat of the hemorrhage was found to be in the right lobe of the liver, which was very much enlarged and was the site of a large softened single tumor, infiltrated with blood and composed of several convoluted nodules measuring about six inches across. No metastases were found in any part of the body.

Primary carcinoma of the liver has been divided into three classes: first, that form occurring with cirrhosis, in which the carcinomatous structures developed from the proliferating bile ducts; second, that form which follows the development of single or multiple adenomata and is clearly developed from the liver cells; third, the variety called diffuse carcinoma of the liver. The specimen presented belonged to this last group. Histological study showed three main types of structure in the tumor, each entirely different from others. First, there were large areas in the tumor which appeared to have developed from a marked increase in number of liver cells with more or less preservation of the liver cords. These cords were composed of an increased number of medium sized cells which were in places associated with huge giant cells. Another characteristic field showed these cords very much increased in width, being composed of six or eight rows of smaller cells separated by cavernous blood channels. A third histological feature visible in some portions of the tumor was the diffuse growth of carcinoma in which the cells were growing irregularly in fibrillated connective tissue, which was itself infiltrated with cells. So that in different portions of this tumor one found three totally different structures. In the first only was there any visible relation to the normal liver structure. The transformation of liver cells into tumor cells was rather sudden; that is, in the length of five or six cells such a change would be found complete. Another feature of this liver which was of interest was the condition of some foci of the parenchyma in the right lobe. In these portions the liver cells, while preserving their relation to the blood vessels showed an enormous increase in size without the neoplastic character. This hypertrophy of the cells was a point about which one

might theorize at considerable length without reaching definite conclusions. It was possible to offer two different interpretations: one might suppose it a preliminary condition preceding the development of the neoplastic hyperplasia; or one might suppose this a type of alteration leading to hypertrophy of the liver cells, but having no relation to the tumor. This latter was Dr. Ewing's opinion, and his chief reason for thinking so was that there were other places where the normal cells seemed to pass more abruptly into tumor cells. One reason for presenting the case was to show that primary carcinoma of the liver does not necessarily exhibit a single characteristic structure.

Discussion.

DR. MANDLEBAUM asked Dr. Ewing whether any cirrhosis existed in this case; or whether there was any ascites or icterus.

DR. EWING said that there had been none whatever.

DR. MANDLEBAUM said that in a case which he was studying at present, large cells such as had been described were quite abundant, and he had looked upon them as regeneration cells which were going on a little further and tending to produce carcinoma cells. Of course, in this case, the cirrhosis was rather marked, and it was well known that regeneration of liver cells was common in such conditions. These cells were seen sometimes bounded on one side by rather normal liver tissue as in the present case. Sometimes they merged slowly into the new growth. Dr. Mandlebaum also asked whether Dr. Ewing had noticed any of the pale cells such as were described about a year ago by Adler, in *Ziegler's Beiträge*, cells rather paler than normal liver cells and supposed to be found principally in infancy as a normal find, and in

adult livers in connection with tumors and cirrhosis, and also in cases of eclampsia.

DR. EWING said that he had not paid particular attention to that point as he was not familiar with the type of cells referred to. As for the liver of eclampsia, there was little relation between the cells seen here and any seen in eclampsia. There were some areas of necrosis, but he had not thought of anything more than an accidental relation between that and the tumor itself. Dr. Ewing had emphasized the large hypertrophic liver cells because there are a number of tumors in which a gradual extension of neoplastic changes is quite evident, especially in early carcinoma of the colon, where one can see every gradation from normal lining epithelium up to tumor cells much increased in size.

DR. MANDLEBAUM said that he had asked particularly about these pale cells as he had noticed in his case that the carcinoma seemed to arise especially from these cells which were lighter than the other cells. These were not easily made out when fixed and stained by the ordinary methods because they then appeared somewhat darker and not readily differentiated from the usual liver cells; but the protoplasm of the cells was quite light and finely granular. The nucleus was not changed. If fixed in osmic acid the light appearance was readily seen. In primary carcinoma of the liver these cells were supposed to be the cells which were involved in the process of the new growth.

DR. O. H. SCHULTZE said that he thought one should proceed with caution when interpreting the occurrence of these large cells. Some inflammatory processes, for instance biliary cirrhosis and true myocarditis, present enormous cells which have no relation to tumor growth. In regard to the giant cells, some time

ago he had had the opportunity of examining a peculiar primary carcinoma of the liver, which from the fusion of the epithelial cells and the formation of enormous multinuclear protoplasmic masses, closely resembled syncytoma malignum. In a case presented to the Society by him some time ago, primary adenocarcinoma of the gall bladder with metastases in the liver, and recently in a case of primary carcinoma of the liver which he had seen through the kindness of Dr. Norris, the same appearance was found.

ANTILEUCOPROTEASE OF BIRDS AND MAMMALS.

EUGENE L. OPIE, M.D., AND BERTHA F. BARKER.

Dr. Eugene L. Opie presented for Miss Barker and himself some experiments on the inhibiting action of the blood serum upon the enzyme contained in the polynuclear leucocytes. As early as 1888, Fr. Müller had demonstrated that the polynuclear leucocytes contained an enzyme which digests proteid best in the presence of an alkaline medium. At a previous meeting of the Society, Dr. Opie had reported a number of experiments which showed that if the cells from a sterile exudate obtained by injecting aleuronat into the pleural cavity of a dog were separated from the serum, they were capable of digesting proteid in either an acid or an alkaline medium. Further experiments demonstrated that two enzymes were present. It was found possible to obtain the enzyme which digests only in the presence of alkali; if the cells of such an exudate were dried there remained only the power to digest in an alkaline or neutral

medium. For this ferment the name of leucoprotease was suggested. The second ferment is present particularly in large mononuclear phagocytes or macrophages, and since these cells are often found in large numbers in the lymph glands the name of lymphoprotease was suggested. This enzyme is inhibited by the normal alkalinity of blood serum and if it were set free in the blood serum by disintegration of cells, its action would be prevented by the alkaline reaction of the serum. At a very early stage in the experiments it was found that the serum of an exudate obtained by injecting aleuronat inhibited the action of that enzyme which digests in alkaline media. If a very small quantity of serum of such an exudate, say, 1 c. c., was brought into contact with dried enzyme, and this allowed to stand at room temperature, the digestion which under ordinary circumstances would occur would be completely prevented. The serum of the blood had the same property as the serum of the exudate. It was found that this inhibiting action was destroyed by a temperature of 75° C. One of the first questions which presented itself was whether this property of inhibiting the action of leucoprotease was common to all the proteids of the serum, perhaps to all the proteid constituents of the body; and these experiments by Dr. Opie and Miss Barker were directed in the first place to determining this question. It is well known that the serum contains a body which inhibits the action of trypsin, an antitrypsin; this anti-enzymotic action is exerted by the albumin fraction of the serum. The various fractions of the serum were separated by well known methods, and it was found that if, say, 20 milligrams of the leucoprotease were allowed to act upon a measured quantity of heated serum, active digestion occurred in the presence of the euglobulin fraction. There was not

only no diminution of digestion but proteolysis was even increased, and the same was true of the pseudoglobulin. But in the presence of the albumin fraction the proteolytic action of the enzyme was completely inhibited. Since it was found not only that the globulin fraction failed to inhibit the action of the ferment, but that it increased the action, it was suggested that the globulin fraction contained a proteolytic enzyme. Appropriate tests demonstrated its presence and showed that the albumin contained none. But since the whole serum is capable of inhibiting the enzymotic action of the leucocyte, the quantity of anti-enzyme more than balances the enzyme contained in the serum.

The next point which presented itself for solution was whether serum other than that of the animal from which the ferment was obtained would inhibit digestion by leucoprotease; that is, for example, whether leucoprotease from the rabbit would be inhibited by serum from the dog as well as from the rabbit and from other animals. If there were a specific relation between the serum of an animal and its own enzymes, evidence would be furnished that the enzymes of different animals were individual. In one series of experiments it was found that a given quantity of leucoprotease from the dog, 20 mgms., was almost completely inhibited by dog's serum, but was inhibited in slightly greater degree by ox serum and human serum. In the second series it was found that the inhibiting action of cat's and goat's serum was considerably greater than that of the dog's own serum. In other experiments it was found that rabbit's serum was far more active than the dog's serum; in other words, dog's serum was less actively anti-enzymotic for dog's own enzymes. Further experiments were necessary to determine if the serum of other animals bears the same

relation to their own enzymes. For this purpose the rabbit was selected. Considerable difficulty was experienced in obtaining a sufficient quantity of leucocytes from the rabbit; aleuronat failed to produce an exudate rich in cells. It was found possible to obtain leucocytes in considerable quantity by injecting turpentine into the subcutaneous tissue of the rabbit. The sera of the dog and rabbit bore exactly the same relation to these enzymes that the same sera bore to the leucoprotease of the dog, that is, the action of the enzyme was inhibited to a greater degree by the rabbit's serum than by that of the dog. This fact suggests that the enzyme in the two animals is of the same character; and that the rabbit's serum contains in larger quantity an anti-enzyme for this leucoprotease which is common to the two species. Previous experiments have shown that the dissolving power of pus is attributable to a loss of this antiferment. The absence of typical suppuration with liquefaction of tissue in the rabbit may be explained by the weak activity of its leucoprotease and the strength of its anti-enzyme.

It was found that the serum of the pigeon and of the hen failed to check the action of leucoprotease of the dog. The possibility then suggested itself that the ferments of the bird might not be identical with those of the mammal. Great difficulty was experienced in obtaining leucocytes in large numbers from the bird, but as previous experiments had shown that the bone marrow of the mammal digests in the presence of alkali more actively than in the presence of acid, the bone marrow of the bird was tested. It was found that the bone marrow of the bird failed to digest in alkaline media, and the same was true of the spleen; both digest only in acid media. These experiments suggest that the leucocytes of the bird do not contain an enzyme which digests in an alkaline medium. It

was possible later to confirm this by direct experiments with exudate. By injections of turpentine into the peritoneal cavity of the hen, a fibrinous exudate very rich in leucocytes was obtained; digestion occurred in acid media but not in neutral or alkaline medium. The leucocytes of the hen do not contain a ferment analogous to the leucoprotease of the mammal, and in correspondence with this fact, the serum of the bird fails to inhibit the leucoprotease of the mammal.

Discussion.

DR. SIMON FLEXNER said that he thought that the explanation which Dr. Opie had offered for the absence of typical suppuration in rabbits was a welcome addition to our knowledge. Everyone who had had to do with rabbits had been struck with the fact that suppuration in these animals, while not infrequent, was not at all typical as compared with suppuration in man and other animals. It had not been clear why this difference existed. If it depended upon the relation between the amount of anti-ferment present in the serum and the capacity of the cells for disintegration, this in itself was an interesting fact. It was just along these lines that the observations of Dr. Opie were extremely promising. He thought that they might eventually throw some light on the factors which determine the different characters of the suppurative process in man. Dr. Flexner asked Dr. Opie whether he had yet determined whether it was possible for a ferment naturally present in the body to attack living tissue and cells, or whether another injurious agent must first cause the death of the cells before the ferment could act. Observations had been made which, on the surface, seemed to indicate that proteolytic ferments could digest

living tissue, but he thought these cases were probably all instances of previous necrosis of cells with subsequent digestion.

DR. JAMES EWING said that he wished to obtain information regarding one or two points in Dr. Opie's work which had been in his mind for some time. As to everyone else, it had been apparent to him that Dr. Opie was dealing with fundamental principles and problems. He had tried to follow the work from the first, and felt, as Dr. Flexner said, that it would eventually clear up many obscure questions. He had been disappointed that Dr. Opie had not been willing to commit himself as to the solution of some of these problems. It would be interesting if he would point out why some forms of chronic edema with few leucocytes take the course they do, and why some exudates reach a point almost of abscess formation and yet never form abscesses. Nothing had been heard from Dr. Opie on the well known condition which had been described as gray induration of the lung, in which there is an exudate composed largely of fibrin or a substance closely resembling fibrin. In this, as was well known, there is no autolysis, the evident reason being that there are not enough leucocytes in the exudate. It would be interesting to determine whether the blood serum or exudate containing large amounts of fibrinogen had any particular influence on the leucocyte emigration and autolysis. Some such factors must determine the failure of the leucocytes to emigrate and digest the fibrin in gray induration. Dr. Opie had explained the failure of abscess formation in rabbits by the existence of much antiferment in rabbit serum. He had pointed out that there was an excessive amount of antiferment in the serum of the rabbit, and that therefore its leucocytes were prevented from dissolving themselves and the tis-

sues in which they lay. Dr. Ewing thought this hardly explained the failure of abscess formation in the rabbit. The softening of the tissues when it occurs must be due to the action of these ferments, but the conditions in the rabbit show that leucocytes are often not attracted to highly irritative foci in sufficient numbers. One could not readily produce a satisfactory purulent peritonitis in a rabbit because here the chemotactic attraction appears to be deficient and the leucocytes are not drawn from the blood in large numbers. If there were instances in the rabbit when the leucocytes gathered in dense foci resembling abscesses and failed to autolyze, then it might be said that this failure was due to the antiferment. Yet abscesses do form in rabbits when the leucocytes are gathered in sufficient numbers, and it would appear that the degree of chemotaxis and emigration must be considered along with the antiferments in the development of abscesses in these animals.

DR. E. LIBMAN introduced the question of the rôle of the ferments in the bacteria themselves in these processes. He brought this subject forth because he had found some years ago that bacteria possessing proteolytic power would lose this property in sugar media. It often happened that infections which in people without diabetes would result in the breaking down of a slough and in subsequent abscess formation, would take a different course in diabetics. The slough would not break down but would be slowly removed like a foreign body, being loosened by a peripheral suppuration. Dr. Libman had thought that this might be brought into relationship with differences in the proteolytic power of the bacteria.

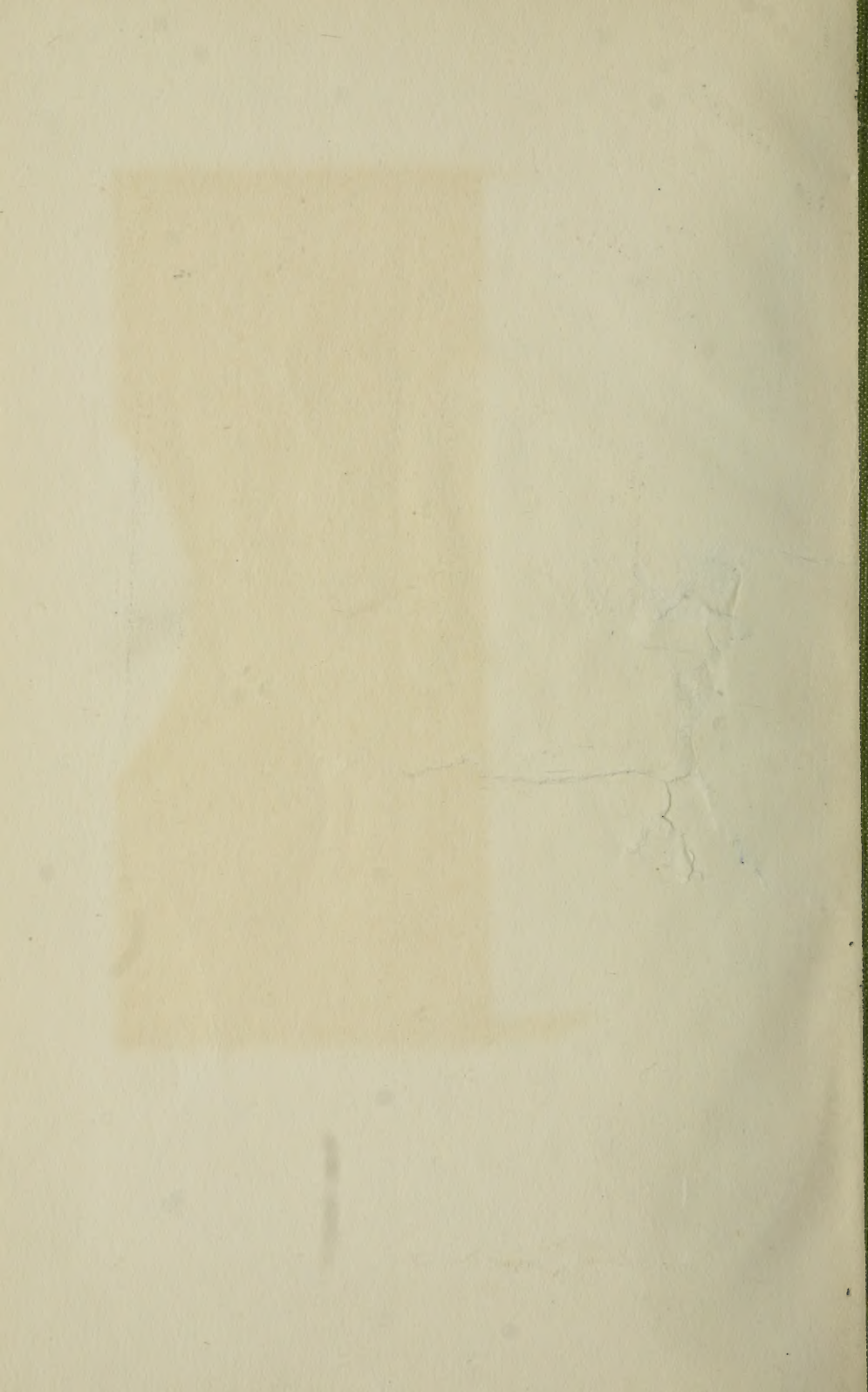
DR. C. W. FIELD asked Dr. Opie whether he had injected any enzymes into dogs to see whether he could increase the antileucoprotease present.

DR. OPIE said with regard to the question asked by Dr. Flexner, as to whether the ferments digest living tissue, that its answer seemed to hinge on the possibility of determining whether a tissue was living or dead when attacked by the ferment. If, for example, the frog's leg is digested in the stomach of the dog, it is necessary to determine whether before the ferments have an opportunity to act the tissue is dead. He did not think that this factor really affected the relation of the enzyme of the leucocytes to suppuration, since it was necessary to accept the fact that necrosis first occurs. The advantage of using turpentine is that it is not a living ferment. When this is injected necrosis first occurs; then an exudate is formed; and abundant fibrin is produced. What is peculiar to the abscess is the solution of fibrin and at least of necrotic tissue, and whether living tissue is attacked by the enzyme is hard to determine. The fact that the enzyme dissolves necrotic tissue and fibrin can be definitely shown, and the experiments which had been mentioned concerned this point rather than whether ferments digest living tissues.

In regard to the special cases spoken of by Dr. Ewing, Dr. Opie could give no better suggestions than those of Dr. Ewing. His experiments had dealt with several specific instances in which inflammation was produced, and he had studied the relation between antibody and enzyme in these particular cases. Of course, where inflammation occurs in a human being and gets to a point where suppuration might be expected but fails to occur, one might suppose that the struggle between the enzyme and the anti-enzyme had been decided in favor of the anti-enzyme. When material obtained by injecting turpentine into the subcutaneous tissue of the rabbit had been tested, polynuclear leucocytes were present in very

great quantity. By injecting aleuronat into the pleural cavity of the rabbit polynuclear leucocytes were obtained in very large number, but in quantity insufficient for the experiments which had been described. Dr. Opie said that he had not attempted to inject leucoprotease into the dog with the purpose of immunizing it, and increasing its antiferment. He had already said that the antileucoprotease is present in the serum of the dog and of all mammals in great quantity, and it would be perhaps difficult to cause its increase. When, however, it had been found that the serum of the bird contained practically no leucoprotease the attempt had at once been made to immunize a hen with the leucoprotease of a dog. The experiment had not been carried very far. Three injections had been made, the largest quantity injected being half a gram, but no increase of antileucoprotease in the serum had been found.

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